Stretch reflex responses in Complex Regional Pain Syndrome-related dystonia are not characterized by hyperreflexia

Winfred Mugge a,⇑, Alfred C. Schouten a,b, Gijsbert J. Bast a, Jasper Schuurmans a, Jacobus J. van Hilten c, Frans C.T. van der Helm a,b

a Biomechanical Engineering, Delft University of Technology, Mekelweg 2, 2628 CD Delft, The Netherlands
b Biomechanical Engineering, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands
c Department of Neurology, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, The Netherlands

1. Introduction

Complex Regional Pain Syndrome type 1 (CRPS) is a disorder that is preceded by a minor to severe trauma to a limb in the absence of an obvious nerve lesion (Veldman et al., 1993; Merskey and Bogduk, 1994), where the severity of symptoms severely affect daily life and cannot be explained by the preceding trauma (Galer et al., 2001).

The acute phase of the syndrome is characterized by pain, sensory symptoms and autonomic features e.g. edema, skin color and temperature changes (Veldman et al., 1993; Schwartzman and Kerrigan, 1990; Birklein et al., 2000; Maihöfner et al., 2007). Afferent feedback
sensory transmission but may also impact on movement control, as illustrated by abnormal sustained muscle contractions (fixed dystonia) that may occur in approximately 25% of the patients with CRPS.

In CRPS patients with dystonia, neurophysiological studies have found disinhibition along the neuraxis (Van de Beek et al., 2002; Schwenkreis et al., 2003; Krause et al., 2004; Eisenberg et al., 2005; Avanzino et al., 2008). Spinal interneuronal circuits mediating presynaptic and reciprocal inhibition have been implicated to play a role in dystonia of CRPS (Van de Beek et al., 2002). Impairment of these circuits may explain the elevated muscle tone or sustained muscle contractions in dystonia (Breakefield et al., 2008). Additionally, Schouten et al. (2003) demonstrated impaired reflex adaptation in CRPS patients with dystonia. Dystonia may respond to the gamma-aminobutyric-acid B (GABA B) agonist baclofen, which inhibits sensory input on neurons of the spinal cord (Van Rijn et al., 2009).

Like in spasticity, disinhibition of reflex pathways may cause motor dysfunction in dystonia of CRPS and interestingly several studies report hyperreflexia on neurological examination of CRPS patients (Schwartzman and Kerrigan, 1990; Birklein et al., 2000). Yet, there is no neurophysiological evidence from direct measurements that quantitatively indicates hyperreflexia in dystonia of CRPS. We therefore evaluated mechanically induced stretch reflex behavior to study if hyperreflexia plays a role in the pathophysiology of CRPS-related dystonia.

2. Materials and methods

2.1. Subjects

Patients (n = 10) diagnosed with CRPS and dystonia (Table 1) were recruited in the Leiden University Medical Center (LUMC). All patients fulfilled the criteria for CRPS-I of the International Association for the Study of Pain (IASP) listed in Table 2 (Merskey and Bogduk, 1994). All patients had fixed dystonia of at least one upper extremity. In the majority of patients dystonia was limited to the distal extremity and mostly involved flexion of digits and wrists in the arms. The presence of dystonia was based on the presence of prolonged muscle contractions resulting in abnormal flexion postures of the hand and fingers. None of the patients had a history of birth trauma or abnormal development. Other causes of dystonia were excluded using appropriate blood tests and imaging studies (computed tomography, magnetic resonance imaging) of the spinal cord and brain. Three CRPS patients without dystonia were included to control for potential effects of pain.

Medication used at the time of the evaluation of reflex responses falls into three categories: antidepressants (6/13), muscle relaxing agents (benzodiazepines or baclofen) (5/13), and pain medication (anticontulvent drugs) (6/13), acetaminophen or NSAID (5/13), and opioids (6/13). At the time of the evaluation three patients were not using medication.

Healthy subjects (n = 10) without any history of neurological disorders and with similar distribution in age and gender as the patients were controls (Table 3). In all patients, measurements were performed on the affected side or in the case of two affected arms, on the dominant one. Measurements of the controls were performed on the dominant arm. All subjects gave informed consent and the ethics committee of the Leiden University Medical Center approved the study.

2.2. Task instruction

Refractive responses are task dependent (Doemges and Rack, 1992a,b). Position tasks (“maintain posture”) result in larger reflexes compared to force tasks (“maintain force”). In general, reflexes are believed to resist unpredictable external perturbations and stabilize the limb. In this study the task instruction is to maintain a force, a task best performed by giving way to the posture perturbations (Mugge et al., 2010). The force task elicits reflex inhibition and would maximize the contrast between controls and patients in case of a lack of inhibition (hyperreflexia).

2.3. Manipulandum

The manipulandum was designed to allow 1D-movement of the subject’s wrist while the subject’s forearm is fixated. An actuator (Baumuller DSM-130N electric motor) was attached to the handle of the manipulandum and applied position perturbations to the subject. The subject was instructed to exert a target force on the handle, as was indicated on a monitor in front of him/her. The axis of rotation was aligned with the wrist flexion-extension axis. The angle (δ) and angular velocity (θ) of the handle, as well as the torque exerted on the handle (T above) were recorded for analysis. Fig. 1 shows a schematic representation of the experimental setup. More detailed information on the manipulandum can be found in previous literature (Schouten et al., 2006). Electromyography (EMG) signals of the flexor carpi radialis (FCR) and extensor carpi radialis (ECR) were recorded using Delsys DE-2.1 electrodes. EMG signals were amplified by a Bagnoli desktop amplifier with a band-pass filter of 20–450 Hz. All signals were captured at a sampling rate of 2500 Hz with 16 bit A/D conversion.

2.4. Experiment protocol

2.4.1. MVC, pain and dystonia

Subjects were instructed to produce a maximum voluntary contraction (MVC) in the flexion and the extension direction, while the handle was fixated in the neutral position of the wrist, i.e. the equilibrium position when relaxed. In three repetitions the MVC torques (T MVC, flex, T MVC, ext) and MVC EMGs (EMG MVC, flex, EMG MVC, ext) were recorded. Three patients demonstrated a drastic reduction in T MVC during the second repetition and were not asked to perform the test a third time, to prevent unnecessary strain. Before and after the experiment, patients were asked to score their pain and dystonia on a Visual Analogue Scale (VAS) with ticks of half a point, where zero represents no pain/dystonia and ten the worst imaginable pain/dystonia (Wewers and Lowe, 1991).

2.4.2. Passive movement

Subjects were instructed to relax the arm muscles, while the handle of the manipulandum moved the wrist into a flexion and an extension posture (three repetitions). Recurrent small steps of 0.03 rad were made at a low velocity of 0.15 rad/s to a maximum of 15° flexion and extension from the neutral position with time intervals of 2.0 s. Steps were sufficiently small and slow to ensure that in the healthy motor control system no reflex activity would be induced. This allowed for evaluation of the background contraction levels at several flexion and extension angles of the wrist.

2.4.3. Reflex measurements

The main part of the experiment required subjects to provide a background contraction of 5% of T MVC, flex in flexion direction. Since reflex responses scale with background contraction, controls additionally performed the task at 1% and 3% T MVC, flex to attain similar torques as patients who have reduced T MVC.

A monitor provided feedback on the exerted and desired torque: a horizontal red bar was displayed, proportionate in length with the torque at the handle; zero length represented no torque while full screen width represented 200% of the desired background torque. In the center of the screen two triangles, just above
2.5.2. Passive movement

Ramp-and-hold position perturbations of 0.05 rad were applied in the extension direction, stretching the flexor muscles. The perturbations were randomly separated in time, however with a minimum of 1.7 s to allow subjects to re-attain the desired background contraction. Power in the EMG-signal after the onset of a stretch perturbation. Power in the EMG-signal was normalized as the cocontractor. To assess the contraction levels of the flexor and extensor muscle.

2.5.4. Cocontraction

The level of cocontraction was determined at the background time window. Since the FCR muscle is exerting a background contraction it is designated as the contractor muscle, and the ECR muscle as the cocontractor. To assess the contraction levels of the muscles, the EMG signals were normalized to maximum voluntary EMG (EMGMVC) as a rough estimate of the cocontraction level, the ratio of extensor background EMG and flexor background EMG (EMG_{BG,ext}/EMG_{BG,flex}) was determined. The standard deviation of the EMG in the background window was determined to assess variability in muscle activation in patients.}

and below the bar, pointed at the desired torque; a blue rectangle ranging from 95% to 105% of the desired torque indicated the target zone. After they had attained the desired torque, the experimenter pressed the start button and a 20-seconds-trial commenced. In every trial five ramp-and-hold position perturbations of 0.05 rad were applied in the extension direction, stretching the flexor muscles. The perturbations were randomly separated in time, however with a minimum of 1.7 s to allow subjects to re-attain the desired background contraction. Ten repetitions of 10 different velocities of the rising part of the ramp were applied ranging from 0.3 to 4.1 rad/s. Ramp velocities were distributed quasi-randomly: each velocity randomly occurred five times in the first 10 trials, and another five times in the second 10 trials. Before starting the main experiment, subjects were given the opportunity to acquaint themselves with the task and the perturbations in training trials. Most subjects were able to perform reasonably well within five training trials.

2.5. Analysis

2.5.1. MVC

$T_{MVC,flex}$ and $EMG_{MVC,flex}$ were calculated as the maximum values of respectively the torque and rectified EMG signals, after filtering with a moving average filter with a 100 ms time window. The highest torque of all repetitions in flexion direction was chosen as $T_{MVC,flex}$ and the corresponding EMG level as $EMG_{MVC,flex}$. As a rough estimate of the cocontraction level, the ratio of extensor background EMG and flexor background EMG (EMG_{BG,ext}/EMG_{BG,flex}) was determined. The standard deviation of the EMG in the background window was determined to assess variability in muscle activation in patients.

Table 1

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Gender</th>
<th>Age [yrs]</th>
<th>Pain</th>
<th>Dystonia</th>
<th>$T_{MVC,flex}$ [Nm]</th>
<th>$T_{MVC,ext}$ [Nm]</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pre [-]</td>
<td>Post [-]</td>
<td>Pre [-]</td>
<td>Post [-]</td>
<td>Anti-convulsants</td>
</tr>
<tr>
<td>P01</td>
<td>M</td>
<td>50</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>2.25</td>
</tr>
<tr>
<td>P02</td>
<td>F</td>
<td>16</td>
<td>8</td>
<td>8</td>
<td>1.5</td>
<td>0.5</td>
<td>7.53</td>
</tr>
<tr>
<td>P03</td>
<td>F</td>
<td>25</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td>7</td>
<td>3.05</td>
</tr>
<tr>
<td>P04</td>
<td>M</td>
<td>42</td>
<td>4</td>
<td>7</td>
<td>0</td>
<td>4</td>
<td>4.08</td>
</tr>
<tr>
<td>P05</td>
<td>M</td>
<td>35</td>
<td>6</td>
<td>7.5</td>
<td>7</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>P06</td>
<td>F</td>
<td>55</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>P07</td>
<td>F</td>
<td>41</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>5.21</td>
</tr>
<tr>
<td>P08</td>
<td>F</td>
<td>56</td>
<td>1.5</td>
<td>1</td>
<td>8</td>
<td>9</td>
<td>0.61</td>
</tr>
<tr>
<td>P09</td>
<td>F</td>
<td>46</td>
<td>10</td>
<td>10</td>
<td>8.5</td>
<td>10</td>
<td>0.26</td>
</tr>
<tr>
<td>P10</td>
<td>F</td>
<td>63</td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>1.46</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.17</td>
</tr>
<tr>
<td>(SD)</td>
<td></td>
<td>(14.5)</td>
<td>(2.63)</td>
<td>(2.48)</td>
<td>(2.95)</td>
<td>(3.14)</td>
<td>(2.42)</td>
</tr>
</tbody>
</table>

CRPS without dystonia

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Gender</th>
<th>Age [yrs]</th>
<th>Pain</th>
<th>Dystonia</th>
<th>$T_{MVC,flex}$ [Nm]</th>
<th>$T_{MVC,ext}$ [Nm]</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>P11</td>
<td>F</td>
<td>28</td>
<td>6.5</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>4.43</td>
</tr>
<tr>
<td>P12</td>
<td>F</td>
<td>42</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>3.09</td>
</tr>
<tr>
<td>P13</td>
<td>F</td>
<td>39</td>
<td>3.5</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>36.3</td>
<td>4.33</td>
<td>5.67</td>
<td>0 (-)</td>
<td>3.51</td>
</tr>
<tr>
<td>(SD)</td>
<td></td>
<td>(7.4)</td>
<td>(1.89)</td>
<td>(2.08)</td>
<td>(0.80)</td>
<td>(1.92)</td>
<td>–</td>
</tr>
</tbody>
</table>

$^a$ Subjectively rated by the subject between 0 and 10 on a Visual Analogue Scale.
The diagnostic criteria for CRPS-I of the International Association for the Study of Pain (IASP) (Merskey and Bogduk, 1994). Criterion 1 is not strictly necessary.

1. Preceding noxious event without (CRPS I) or with observable nerve lesion (CRPS II)
2. Spontaneous pain or hyperalgesia/hyperesthesia not limited to a single nerve territory and disproportionate to the initiating event
3. Edema, skin blood flow (temperature) or sudomotor abnormalities, motor symptoms or trophic changes are present in the affected limb, in particular at distal sites
4. Other diagnoses are excluded

### Table 2
Control information.

<table>
<thead>
<tr>
<th>Control #</th>
<th>Gender</th>
<th>Age [yrs]</th>
<th>MVC,flex [Nm]</th>
<th>MVC,ext [Nm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>C01</td>
<td>F</td>
<td>33</td>
<td>8.75</td>
<td>5.99</td>
</tr>
<tr>
<td>C02</td>
<td>M</td>
<td>50</td>
<td>15.72</td>
<td>10.24</td>
</tr>
<tr>
<td>C03</td>
<td>F</td>
<td>48</td>
<td>5.95</td>
<td>2.35</td>
</tr>
<tr>
<td>C04</td>
<td>F</td>
<td>50</td>
<td>16.64</td>
<td>9.12</td>
</tr>
<tr>
<td>C05</td>
<td>F</td>
<td>52</td>
<td>5.34</td>
<td>4.79</td>
</tr>
<tr>
<td>C06</td>
<td>F</td>
<td>52</td>
<td>9.87</td>
<td>7.27</td>
</tr>
<tr>
<td>C07</td>
<td>F</td>
<td>56</td>
<td>9.87</td>
<td>7.19</td>
</tr>
<tr>
<td>C08</td>
<td>F</td>
<td>29</td>
<td>9.65</td>
<td>5.92</td>
</tr>
<tr>
<td>C09</td>
<td>F</td>
<td>27</td>
<td>9.11</td>
<td>5.79</td>
</tr>
<tr>
<td>C10</td>
<td>F</td>
<td>25</td>
<td>9.1</td>
<td>4.48</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>40.3 (11.91)</td>
<td>9.72 (3.81)</td>
<td>6.31 (2.28)</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. Schematic representation of the experimental setup. The subject is seated in upright position with his/her forearm fixed and unimpeded movement of the wrist. The actuated handle induces wrist rotations to the subject since the axis of rotation of the handle is aligned with the wrist flexion/extension axis.

### 2.6. Statistics

The effects of ramp velocity and group on the response amplitudes $A_{M1}$ and $A_{M2}$, and the reflex latencies were tested with a two-way repeated measures analysis of variance (RM-ANOVA). The effect of group on $T_{MVC}$ was tested in independent sample $t$-tests and (pre- vs post-) effects of participation on pain and dystonia were tested in paired $t$-tests. Group effects in EMG activity and cocontraction level between controls and patients were tested in one-way ANOVA’s and within controls a repeated measures ANOVA was used to compare EMG activity and cocontraction level at several background contraction levels. A significance level of 0.05 was used.

### 3. Results

#### 3.1. Pain and dystonia VAS scores and MVC torques

Tables 2 and 3 give an overview of the pain and dystonia Visual Analogue Scale measurements, age and $T_{MVC}$ of patients and controls. The $T_{MVC}$ was substantially lower in CRPS patients with dystonia compared to controls ($T_{MVC,flex}$: $t(18) = 4.59, p < 0.001$ and $T_{MVC,ext}$: $t(18) = 4.84, p < 0.001$). Pain and dystonia VAS scores and $T_{MVC}$ in CRPS patients without dystonia were within 1 standard deviation of the CRPS patients with dystonia.

#### 3.2. Passive movement

Only one of the patients demonstrated substantial wrist muscle EMG activity and considerable torque at the handle during the passive movement. Typically no EMG activity over background was detected. Fig. 2 shows a typical example of EMG and torque during the passive movement for both controls and patients. Additionally, the single subject that did exert an active flexion torque during extension of the wrist is indicated (P09).

#### 3.3. Reflex measurements

Fig. 3 presents the flexor EMG of a typical subject in response to a ramp-and-hold perturbation (3.9 rad/s). For the flexor EMG, ramp velocity increased the $M1$ magnitude ($A_{M1}$) in controls and patients ($F(1.18,10.56) = 16.321, p < 0.001$) and within controls a significant effect of background contraction level ($F(2,18) = 8.63, p < 0.01$) and a significant correlation of velocity and background contraction level on the $M1$ magnitude ($A_{M1}$) was found ($velocity \times contraction level: F(3.35,30.15) = 4.94, p < 0.01$).

Fig. 4 presents the normalized $M1$ response against ramp velocity and demonstrates that the reflex size decreased with background contraction level. The repeated measures ANOVA including the patients with dystonia revealed a significant group effect ($F(1.28,11.48) = 5.93, p < 0.05$). Post hoc tests revealed a significantly smaller normalized reflex size in patients with dystonia compared to controls performing at a background contraction level of 1% of $T_{MVC}$ ($p < 0.05$).

Fig. 5 presents the reflex onset time of the $M1$ response ($t_{M1}$) against ramp velocity. The $t_{M1}$ decreased with ramp velocity in controls and patients ($F(2,79,25.12) = 40.58, p < 0.001$) and within controls a significant effect of background contraction level was found ($F(2,18) = 5.28, p < 0.05$). Post hoc tests of the repeated measures ANOVA revealed a significantly later reflex onset in controls performing at 1% background contraction level than when performing at 5% background contraction level ($p < 0.05$). The later reflex onset in patients compared to controls at 5% background contraction level did not reach significance ($p = 0.061$).

For controls a similar pattern can be discerned for the $M2$, as presented in Fig. 6: the normalized reflex size decreased with background contraction level ($F(2,18) = 24.01, p < 0.001$), but ramp velocity did not reach significance level ($F(2.46,22.16) = 2.57, p = 0.089$). The $M2$ magnitude ($A_{M2}$) is equal or smaller than the $M1$ magnitude ($A_{M1}$) depending on ramp velocity. As the $M2$ magnitude in patients lies between that of the controls at 1% and 3% background contraction, no significant difference between the patients with dystonia and controls at 1%, 3% and 5% background contraction was found.

Also in the extensor, shortened by the ramp position perturbation, a significant effect of group ($F(3.27) = 4.89, p < 0.01$) and ramp velocity ($F(3.13,28.19) = 3.25, p < 0.05$) was found on EMG in the $M1$ window. Post hoc tests revealed significantly less normalized EMG activity in the $M1$ window for patients with dystonia with respect to controls at 3% ($p < 0.05$) and 5% background contraction level ($p < 0.01$). In the $M2$ window at the extensor a significant effect of group was found ($F(3.27) = 3.26, p < 0.05$). Post hoc tests revealed that the EMG activity in patients with dystonia was only less with respect to the controls performing at 1% background contraction level ($p < 0.05$).
3.4. Cocontraction

Within the controls flexor background torque increased the activity of the flexor ($F(1.18,10.62) = 13.69$, $p < 0.01$) and decreased the EMG-ratio or cocontraction measure ($F(1.11,9.95) = 21.84$, $p < 0.001$). No significant effect of contraction level was found on extensor background EMG ($F(1.04,9.39) = 2.91$, $p = 0.120$).

The standard deviation of the flexor EMG in the background window was significantly larger in patients with dystonia than in controls at 1% background contraction ($p < 0.05$) and the standard deviation of the extensor EMG was significantly larger than in controls at any background contraction level (all $p < 0.05$).

The oneway ANOVA revealed a significant effect of EMG-ratio ($F(3,36) = 9.04$, $p < 0.001$). The raw EMG levels presented in Fig. 7 show that patients with dystonia have substantially more activity in the extensor ($EMG_{ext}$) than the controls at any of the background contraction levels (all $p < 0.05$). According to post hoc tests with Bonferroni-correction, the EMG-ratio was significantly higher for the patients with dystonia compared to controls at 3% ($p < 0.01$) and 5% ($p < 0.001$) background contraction. In controls, a lower level of background torque led to an increase in cocontraction level, up to equal activity of flexor and extensor muscles with a background contraction of 1% of $T_{MVC}$. Despite that the cocontraction level was close to unity, a net flexion torque was produced since the flexor muscle exerted higher forces at equal EMG-level than the extensor muscle.

For flexor and extensor background EMG and EMG-ratio, the patients without dystonia (not presented in the figure) showed similar values as the controls at 3% background contraction.

4. Discussion

In this study we investigated wrist motor dysfunction in subjects with CRPS-related dystonia. Three experiments were performed: (1) maximum voluntary contraction torque, (2) resistance against slow passive movement, and (3) rapid muscle contraction.

![Fig. 2. Example recordings of the passive movement experiment. The black line represents a typical recording of a control, showing no EMG activity during the passive movement. The gray line represents the recording of one patient (P09) that did demonstrate substantial EMG activity and considerable torque at the handle. All other patients resembled the controls. The panels show, from top to bottom: the relative angle of the handle/wrist to the neutral position ($\theta$), torque exerted to the handle ($T_{\text{handle}}$), flexor EMG, and extensor EMG. EMG signals have been normalized to maximum voluntary contraction ($EMG_{\text{MVC}}$) and torque and EMG signals have been smoothed with a moving average filter with a 100 ms time window.](image1)

![Fig. 3. Example recording of a ramp-and-hold perturbation with a ramp velocity of 3.9 rad/s. Top: the relative angle of the handle/wrist to the neutral position ($\theta$); middle: angular velocity of the handle/wrist ($\dot{\theta}$); bottom: flexor EMG, normalized to background EMG. Light gray area designates the M1 time window (from 20 to 55 ms after perturbation onset) and the dark gray area designates the M2 time window (from 55 to 100 ms after perturbation onset). $t_{M1}$ indicates the onset time of the M1 response and $A_{M1}$ and $A_{M2}$ the magnitudes of the M1 and M2 response, respectively (mean amplitude of EMG).](image2)
The stretch reflex is a fundamental property of the human nervous system that is involved in the regulation of muscle tone and reflexive movement. It is elicited by the sudden stretch of a muscle and is characterized by a burst of activity in motor units that innervate the stretched muscle. This reflex response is mediated by the monosynaptic reflex arc, which consists of a single synaptic junction between the afferent (sensory) neuron and the efferent (motor) neuron. The reflex response is triggered by the activation of sensory receptors in the muscle that detect the stretch and send a signal to the spinal cord via the peripheral nerve. The spinal cord then processes the signal and sends a motor command to the muscle via the appropriate motor neurons.

The magnitude and latency of the stretch reflex can vary depending on the characteristics of the stimulus, the state of the muscle, and the condition of the individual. In some cases, the reflex response may be enhanced or diminished, leading to changes in muscle tone and movement. For example, in patients with neurological disorders such as stroke or spinal cord injury, the stretch reflex may be exaggerated or absent, leading to deficits in motor function. In other cases, the reflex response may be reduced or abolished, leading to a loss of protective reflexes and increased risk of injury.

The stretch reflex is an important mechanism for maintaining posture and balance. It also plays a role in the regulation of muscle tone and the prevention of muscle spasm. However, in some cases, the reflex response may become uncontrollable and lead to spasticity or dystonia, which can result in significant physical and functional impairments.

In conclusion, the stretch reflex is a fundamental property of the nervous system that is involved in the regulation of muscle tone and reflexive movement. Understanding the mechanisms underlying the stretch reflex is important for the diagnosis and treatment of neurological disorders that affect the function of the nervous system.

Fig. 4. M1 magnitude in the flexor muscle (mean amplitude of the flexor EMG from 20 to 55 ms after perturbation onset) as a function of ramp velocity. The gray traces represent the controls at background contraction levels of 1% (dotted), 3% (dashed), and 5% (solid) of MVC torque (T_MVC) and the black trace represents the CRPS-patients with dystonia at 5% T_MVC. M1 magnitudes are normalized to background EMG (mean amplitude of flexor EMG of the 200 ms before perturbation onset) and averaged over all repetitions and subjects. Error bars indicate group standard errors of the mean. The fact that the standard errors of the mean in the patient group match those of the control groups is indicative for equivalent task execution.

Fig. 5. M1 onset time in the flexor muscle (first point in time where EMG exceeded background level by more than 3 SD) as a function of ramp velocity. The gray traces represent the controls at background contraction levels of 1% (dotted), 3% (dashed), and 5% (solid) of MVC torque (T_MVC) and the black trace represents the CRPS-patients with dystonia at 5% T_MVC. M1 onset times are averaged over all repetitions and subjects. Error bars indicate group standard errors of the mean.

Fig. 6. M2 magnitude in the flexor muscle (mean amplitude of the flexor EMG from 55 to 100 ms after perturbation onset) as a function of ramp velocity. The gray traces represent the controls at background contraction levels of 1% (dotted), 3% (dashed), and 5% (solid) of MVC torque (T_MVC) and the black trace represents the CRPS-patients with dystonia at 5% T_MVC. M2 magnitudes are normalized to background EMG (mean amplitude of flexor EMG of the 200 ms before perturbation onset) and averaged over all repetitions and subjects. Error bars indicate group standard errors of the mean.
ground contraction. The M2 magnitude in patients lies between the M2 magnitudes for controls at 1% and 3% background contraction. These findings and the fact that the mean \( T_{\text{MVC}} \) in patients was a factor three lower than in controls, suggest that the reflex responses of patients should be compared to the controls at the absolute torque level, in this case closest to 1% background contraction. At 5% background contraction there are no significant differences in the M1 and M2 reflex size between patients and controls. However, at 1% background contraction, the M1 responses in CRPS-patients with dystonia are smaller than those in the controls, which does not corroborate with the characteristics of hyperreflexia but is in line with Grünewald et al. (1997) who reported abnormal perception of limb velocity (subserved by \( I_a \) afferents) and essentially normal perception of limb position (subserved by \( II_a \) afferents) in patients with focal dystonia.

Although the patients were highly motivated, the possibility of a reduced \( T_{\text{MVC}} \) due to pain cannot be excluded. We therefore evaluated three CRPS patients without dystonia. These patients had similar \( T_{\text{MVC}} \) values as patients with dystonia, indicating that the reduced \( T_{\text{MVC}} \) in patients is not inherent to dystonia. If the \( T_{\text{MVC}} \) was limited by pain, the muscles of these patients should still be capable of producing higher torques than the currently measured \( T_{\text{MVC}} \). This may be another reason why comparison of patients with controls at lower background contraction levels may be feasible, since the higher the actual maximum voluntary contraction torque in patients, the lower the actual percentage \( T_{\text{MVC}} \) the patients delivered at the desired background contraction level.

In conclusion, the results of this study show no evidence that hyperreflexia is the main abnormality of reflex behavior at the wrist in CRPS-patients with dystonia. Although several concerns arise when comparing patients to controls, the results seem to suggest hyporeflexia rather than hyperreflexia. Traditionally, hyporeflexia is associated with a lower motor neuron deficit, whereas hyperreflexia is often attributed to upper motor neuron lesions (Gowers, 1886). Hyporeflexia is usually noted in myopathies like muscular dystrophy and polymyositis even when strength is only moderately impaired and almost always in patients with motor neuropathy, whether axonal or demyelinating (Ellis, 1994). The indication of hyporeflexia may therefore provide new insights into the pathophysiology of CRPS-related dystonia.

We hypothesize that hyporeflexia results from compensation for the dystonia by indiscriminate descending inhibition to the motor system, which correlates to trends observed in previous work (Schouten et al., 2003). If dystonia is caused by aberrant reflexes, the mechanism is not as simple as suggested in literature and may involve reflex circuitry other than the muscle spindle stretch reflex, like Golgi tendon organ activity. Modeling studies provide evidence for involvement of abnormal Golgi tendon organ activity in fixed dystonia (Mugge et al., in preparation; Munts et al., 2011) and may contribute to unravel the mechanisms underpinning dystonia and focus further research.

**Acknowledgments**

This study was performed within TREND (Trauma Related Neuronal Dysfunction), a knowledge consortium that integrates research on Complex Regional Pain Syndrome type I. The project is supported by a Dutch Government Grant (BSIK03016). Conflict of interest: The authors declare not to have any commercial associations that might pose a conflict of interest in connection with the article.

**References**


Chui WT, Sanger TD. Force variability during isometric biceps contraction in children with secondary dystonia due to cerebral palsy. Mov Disord 2009;24(9):1299–305.


