

WITHDRAWAL REFLEXES IN THE UPPER LIMB ADAPT TO ARM POSTURE AND STIMULUS LOCATION

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ABSTRACT: *Introduction:* Withdrawal reflexes in the leg adapt in a context-appropriate manner to remove the limb from noxious stimuli, but the extent to which withdrawal reflexes adapt in the arm remains unknown. *Methods:* We examined the adaptability of withdrawal reflexes in response to nociceptive stimuli applied in different arm postures and to different digits. Reflexes were elicited at rest, and kinetic and electromyographic responses were recorded under isometric conditions, thereby allowing motoneuron pool excitability to be controlled. *Results:* Endpoint force changed from a posterior–lateral direction in a flexed posture to predominantly a posterior direction in a more extended posture [change in force angle (mean \pm standard deviation) $35.6 \pm 5.0^\circ$], and the force direction changed similarly with digit I stimulation compared with digit V (change = $22.9 \pm 2.9^\circ$). *Conclusions:* The withdrawal reflex in the human upper limb adapts in a functionally relevant manner when elicited at rest.

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The activation of nociceptive afferents elicits reflexes that provide a safety margin from noxious stimuli by initiating actions to withdraw the limb prior to stimulus perception. Early reports characterized the withdrawal reflex as a “flexion reflex,” because stimulation of afferents in the cat hindlimb predominantly evoked excitation of flexor muscles and inhibition of extensor muscles, resulting in flexor movements at the joints.¹ Reports of exceptions to the “flexion reflex,” including excitatory responses in extensor muscles in some conditions,^{1–4} preceded more recent studies demonstrating a functional organization of withdrawal reflexes in the animal hindlimb^{5–8} and the human lower limb.^{9,10} Such an organization allows for flexibility (i.e., functional adaptation) in the motor actions initiated by the withdrawal reflex to avoid noxious stimuli. Withdrawal reflexes in the upper limb have not been examined in

the same detail as those in the lower limb. Although spinal and supraspinal pathways undoubtedly contribute to the control of both limbs, there is evidence for increased spinal contributions for the legs^{11,12} and supraspinal contributions for the arms.^{13,14} Furthermore, the legs are often used in constrained or repetitive tasks, such as stance¹⁵ and locomotion,^{16–18} whereas the actions of the arms are often less stereotyped. Hence, it is unclear whether the flexibility demonstrated for the withdrawal reflex in the lower limb is also present in the upper limb. Quantifying the adaptability of the upper limb withdrawal reflex is a necessary step toward understanding automatic control of the upper limb in response to noxious stimuli and how this control may be altered after injury.

Withdrawal reflexes in the human upper limb have been shown to adapt to the different phases of movement^{19–21} and to stimulus location^{22,23} and elbow position.²⁴ All studies cited here were performed in the presence of volitional contractions and have shown task-dependent changes in excitatory and inhibitory responses to the noxious stimulus. These important studies demonstrate that some flexibility is possible, but they were not designed to control the excitability of the motoneuron pool, which can have a major influence on reflex behaviors.²⁵ Isometric experiments with reflexes elicited from muscles at rest can control the excitability of the motoneuron pool and reduce the influence of proprioceptive feedback on the withdrawal response. The few studies that have examined muscle activity,²⁶ muscle activity and kinematics,^{21,27} or kinetics²⁸ of the upper limb withdrawal reflex at rest in response to digital nerve stimulation have considered only a single starting posture; only 1 study was done under isometric conditions.²⁸ All studies reported that the flexor and extensor muscles of the arm were excited in response to a noxious stimulus and that the withdrawal response involved flexion of the elbow. Concurrent activation of flexor and extensor muscles and differences in movements at the wrist and shoulder^{21,27} suggest that these activities may be tuned to account for

Abbreviations: AD, anterior deltoid; ANOVA, analysis of variance; BIC, biceps brachii; BRD, brachioradialis; CCU, constant current unit; EMG, electromyography; MVC, maximum voluntary contraction; PD, posterior deltoid; SIU, stimulus isolation unit; TRI, lateral head of the triceps brachii

Key words: endpoint force; fingertip stimulation; humans; motor control; nociceptive; spinal reflexes

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different starting postures and stimulus locations, as has been demonstrated for the lower limb.²⁹⁻³¹

The purpose of this study was to determine whether the withdrawal reflex adapts to different stimulus locations and postures in the upper limb. Kinetic and electromyographic (EMG) responses to nociceptive stimuli delivered to the digits with the arm muscles at rest were recorded when the arm was constrained to 3 different postures and by stimulation of 3 different digits in a single posture. We hypothesized the withdrawal reflex would be appropriate to move the limb away from the stimulus in all conditions. Such results would demonstrate the flexibility of this basic reflex as a mechanism for protecting the upper limb against injury.

METHODS

Participants. Twenty-two healthy adults [10 men and 12 women, age (mean \pm SD) 28.2 ± 3.0 years] without history of neurological disorder or upper limb impairment were recruited and provided informed consent prior to participation. The protocol was approved by the institutional review board of Northwestern University (2643-002).

Force Recordings. Subjects were seated comfortably in an upright chair with the right forearm secured in a plastic cast and supported against gravity (Fig. 1A). The cast was connected at the wrist to a 6 degree-of-freedom force transducer (67M25; JR-3, Woodland, California). This device was mounted on a rotational bearing that prevented any moments from being generated in the horizontal plane. The resulting forces measured at the wrist are reported in the coordinate system shown in Figure 1B.

Electromyography. Surface EMG data were recorded from disposable bipolar electrodes (Noraxon USA, Inc., Scottsdale, Arizona) located over the brachioradialis (BRD), long head of the biceps brachii (BIC), lateral head of the triceps brachii (TRI), anterior deltoid (AD), and posterior deltoid (PD). The skin overlying each muscle belly was cleaned and abraded prior to electrode placement. EMG signals were amplified and conditioned using an EMG system (AMT-8; Bortec Biomedical, Ltd., Calgary, Alberta, Canada) with high- and low-pass cut-off frequencies of 10 and 1000 Hz, respectively. The resulting signals were anti-alias filtered using a fifth-order Bessel filter with a cut-off frequency of 500 Hz and sampled at 2.5 kHz for subsequent analysis.

Stimulation Conditions. The digits of the hand were stimulated using a Grass stimulator (Model S48; Grass Technologies, Astro-Med, West Warwick, Rhode Island) connected in series with a stimulus isolation unit (SIU-5) and a constant current unit (CCU-1). Short trains of stimuli were delivered to

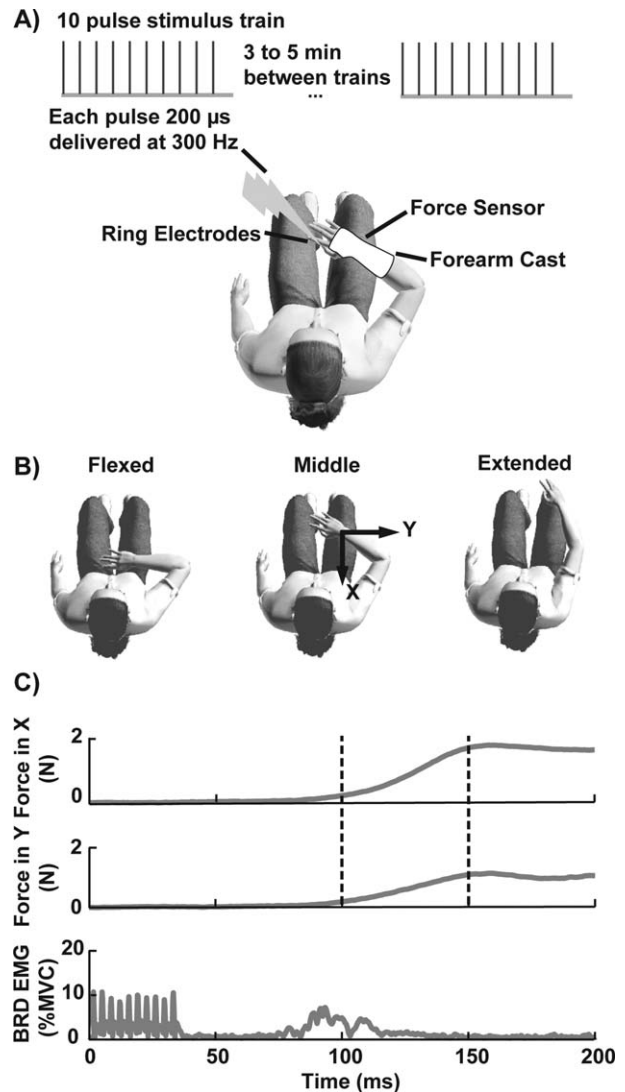


FIGURE 1. (A) Experimental set-up and stimulus parameters. A force sensor was connected to the cast at the wrist. Stimulus trains were delivered while the arm was supported against gravity. (B) The effect of posture was tested by recording withdrawal reflexes with digit II stimulation in 3 postures: Flexed; Middle; and Extended. Forces and torques were measured at the center of the force sensor according to the coordinate system shown. (C) Average force responses in the X and Y directions and average EMG response for the brachioradialis (BRD) across trials for a representative subject in the Middle posture condition. Resultant force angles and magnitudes were computed for each trial from the X and Y components of the force occurring 50 ms after the first detectable change (dashed lines).

the distal parts of digits using stainless-steel ring electrodes while the subject was relaxed. Each stimulus train consisted of ten 200-μs pulses, delivered at 300 Hz, which was consistent with previous studies of withdrawal reflexes in the upper limb at rest.²⁷ Stimulation intensity was increased slowly to determine perceptual threshold at the beginning of the experiment. It was then increased in 2-mA steps until the pain threshold was exceeded and the subject reported that further increases were intolerable. The typical stimulus intensity for the

experiments was set at 40–50 mA, which was similar to intensities used in previous studies of the upper limb.^{22,24,28} The stimulus trains used to elicit the reflex response during the experimental protocols were delivered at random intervals of 3–5 min. Eight to 10 stimulus trains were delivered in each experimental condition, and the stimulation intensity was kept constant across all conditions for a given subject.

Protocols. Withdrawal reflexes were tested in 9 subjects (4 men and 5 women, age 28.8 ± 4.3 years). Subjects were assessed with the standard 2-point discrimination test³² and had normal sensory function (≤ 5 mm) in the right thumb (digit I), index finger (digit II), and pinky finger (digit V). At the beginning of each test session, subjects performed maximum voluntary contractions (MVCs) in elbow flexion and extension and shoulder flexion and extension. The maximum voluntary EMG was computed as the mean of the rectified EMG for 0.5 s around the peak for each muscle and was used to normalize the EMG recorded during withdrawal reflex trials.

The first block of experiments tested the influence of arm posture on withdrawal reflexes with stimuli applied to digit II. Withdrawal reflexes were tested in 3 postures: flexed posture (Flexed; elbow flexion $139 \pm 12^\circ$, shoulder flexion $17 \pm 12^\circ$, shoulder abduction $78 \pm 6^\circ$); midrange posture (Middle; elbow flexion $93 \pm 6^\circ$, shoulder flexion $42 \pm 10^\circ$, shoulder abduction $64 \pm 6^\circ$); and extended posture (Extended; elbow flexion $51 \pm 8^\circ$, shoulder flexion $43 \pm 13^\circ$, shoulder abduction $78 \pm 4^\circ$) (Fig. 1B). Joint angles were measured at random intervals throughout the trial blocks to ensure there was no unintended change in arm posture. The order in which each arm posture was tested was randomized across subjects. The second block of experiments evaluated the influence of stimulus location on withdrawal reflexes. In this block, all measurements were made with the arm in the Middle posture. Digits I, II, and V were stimulated, with the order of digit randomized across subjects. The order of experiment blocks (i.e., posture and digit) was also randomized for each subject.

A separate set of control experiments were performed on 9 subjects (6 men and 3 women, 28.6 ± 3.7 years; 5 subjects also participated in the withdrawal reflex protocol) to evaluate voluntary reaction time in response to non-nociceptive electrical stimulation. Subjects were instructed to voluntarily withdraw the arm as quickly as possible in response to a single-pulse stimulus. Stimulus intensity was set below pain threshold (~ 4 times perceptual threshold), and the stimulus was applied to digit II with the arm in the Middle posture. Subjects were

instructed to pull the hand back in a line toward the ipsilateral shoulder as quickly as possible.

We also conducted a control experiment in 10 subjects (4 men and 6 women, 28.1 ± 1.9 years; 1 subject also participated in withdrawal reflex and voluntary reaction protocols) to evaluate changes in the perceptual threshold across arm postures and stimulus locations. Perceptual threshold was determined to be the lowest stimulus intensity at which subjects could perceive the stimulus train (10 200- μ s pulses, delivered at 300 Hz).

Data Analysis. Force analyses were confined to the horizontal (X–Y) plane, because forces in the vertical direction were not significantly different across conditions. Resultant force directions and magnitudes were computed from the initial linear region of the measured force trajectories (Fig. 1C). The linear force region was determined via visual inspection for each trial and began, on average, 106.4 ± 13 ms after stimulus onset and lasted 48.9 ± 9 ms across subjects and conditions. Based on visual inspection, the endpoint force resulting from the elicited reflex was quantified as the force occurring 50 ms after first detectable change due to the noxious stimulation, termed the force onset. The force onset for each trial was identified as the time when the force (either X or Y component) exceeded 3 standard deviations above the mean of the background force. Background force was computed 250 ms before stimulation onset.

EMG signals were processed by first removing the mean of each signal to offset the overall average to zero. The EMG signals were then rectified and normalized to the maximum voluntary EMG recorded for each subject. Reflex and voluntary EMG latencies (i.e., time from stimulus onset to EMG onset) were computed to define time windows for quantifying reflex responses. EMG latencies for each reflex and voluntary trial were determined as the time when the EMG exceeded 3 standard deviations above the mean background EMG measured from a period of 100 ms prior to stimulation for each muscle. Reflex EMGs for each trial were then quantified as the average rectified EMG computed over a 50-ms window after EMG onset.

Statistical Analysis. Linear mixed-effect models and analysis of variance (ANOVA) were used to compare the direction and magnitude of the reflex forces elicited across all postures using R software (R Foundation for Statistical Computing, Vienna, Austria). Separate linear mixed-effect models and analyses of variance were used to test for differences in the corresponding reflex EMG magnitudes across arm postures. Arm posture was considered as an independent factor and subject as a random factor. The inverse of the group variances were

included as weights in the linear mixed-effect models to account for unequal variances across postures. The same analysis was repeated for the second experiment, in which the digit stimulated was treated as an independent factor and subject as a random factor. *Post hoc* comparisons were performed when *F*-tests for the main effect of posture or digit were significant. Separate ANOVAs were used to determine the influence of the experimental condition (i.e., reflex or voluntary trial) on the EMG and force latencies. In these analyses, condition was an independent factor, and subject was a random factor. Finally, ANOVAs were used to determine the influence of arm posture and digit stimulated on perceptual threshold. Results were considered significant if $P < 0.05$.

RESULTS

Effect of Arm Posture on Withdrawal Reflex Response. The direction of the endpoint force elicited by the withdrawal reflex varied significantly with changes in arm posture [$F_{(2,205)} = 31.1$, $P < 0.0001$; Fig. 2A]. As the arm was moved from the Flexed to the Extended posture, there was a

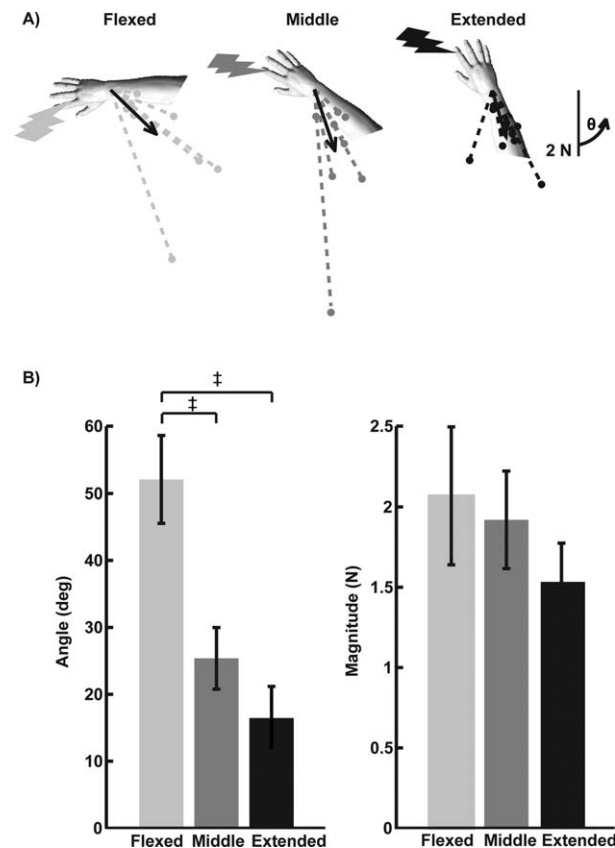


FIGURE 2. (A) Average force vectors across trials for each subject (dotted lines) and across subjects (black arrow) in each of the posture conditions. (B) Average force response angles (left) and magnitudes (right) across subjects in the 3 posture conditions with significant differences between postures denoted by ‡ $P < 0.001$. Error bars are \pm standard error.

consistent change in the withdrawal force from being oriented in the posterolateral direction to predominantly the posterior direction (Fig. 2A). The posture-dependent change in force direction was significant between the flexed posture and both of the more extended postures, but the difference between the Middle and Extended postures was not significant (Fig. 2B). In contrast to the posture-dependent change in force direction, the magnitude of the same forces evoked by the withdrawal reflex did not vary significantly with posture.

The muscle activations elicited by the withdrawal reflex also varied significantly with arm posture (Fig. 3) for the BRD [$F_{(2,205)} = 12.1$, $P < 0.0001$], BIC [$F_{(2,205)} = 15.2$, $P < 0.0001$], TRI

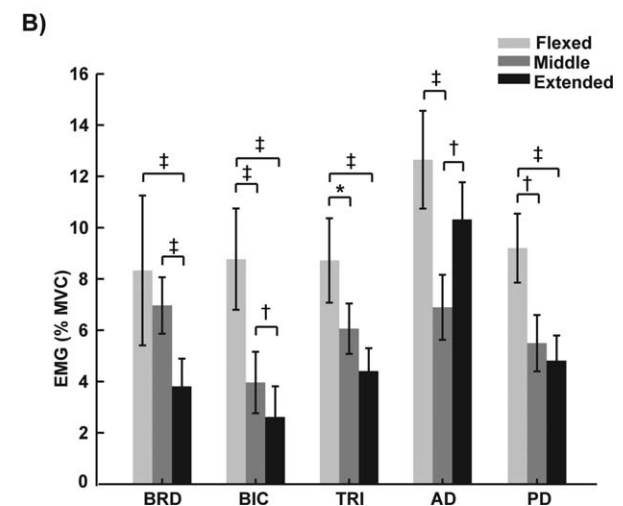
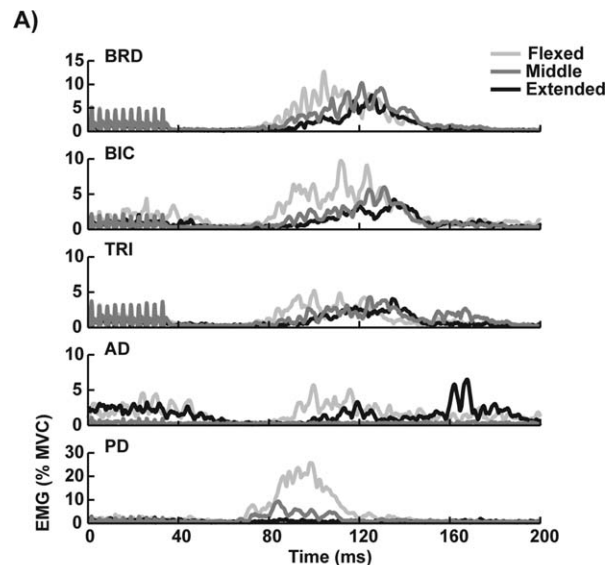


FIGURE 3. (A) Average EMG across trials for a representative subject in the 3 posture conditions. Stimulus artifacts were present as trains were delivered from 0 to 33 ms. (B) Average EMG responses across subjects in the 3 posture conditions with significant differences between postures denoted by: * $P < 0.05$; † $P < 0.01$; and ‡ $P < 0.001$. Error bars are \pm standard error.

[$F_{(2,205)} = 12.1$, $P < 0.0001$], AD [$F_{(2,205)} = 11.8$, $P < 0.0001$], and PD [$F_{(2,205)} = 10.2$, $P < 0.0001$]. Across muscles, the most consistent finding was that the EMG responses were largest in the Flexed posture. EMG responses in the Flexed posture were significantly greater than those in the Middle posture for all muscles except the BRD; they were also significantly greater than those in the Extended posture, except for the AD. The EMG response was significantly greater in the Middle posture relative to the extended posture for the BRD, whereas the EMG response was significantly greater in the Extended posture relative to the Middle posture for the AD only. These posture-dependent changes in EMG suggest that the posture dependence observed in the endpoint forces was not only due to changes in limb biomechanics but also to how the nervous system activated the arm muscles at each posture. However, the changes may also be attributed in part to posture-dependent changes in the EMG recordings (i.e., the position of the recording electrode on the muscle changes with posture). To control for that possibility, we also examined the influence of changes in stimulation location with the arm at a fixed posture.

Effect of Digit Stimulation on Withdrawal Reflex Response. With the arm fixed at the Middle posture, the digit of the hand that was stimulated (I, II, or V) had a significant effect on the direction [$F_{(2,205)} = 43.5$, $P < 0.0001$] and magnitude [$F_{(2,205)} = 19.5$, $P < 0.0001$] of the endpoint force response (Fig. 4). As the stimulus was moved from digit I to V, there was a consistent change in the orientation of the endpoint force from the posterolateral direction to predominantly the posterior direction (Fig. 4A). The digit-dependent change in orientation of the force response was significant between digits I and II, between digits I and V, and between digits II and V (Fig. 4B). The magnitude of the force response from the withdrawal reflex was significantly greater with stimulation of digit V compared with both digits I and II (Fig. 4B).

The muscle activations elicited by the withdrawal reflex also varied significantly with changes in the digit stimulated (Fig. 5). Significant variations were observed for the BRD [$F_{(2,205)} = 28.3$, $P < 0.0001$], BIC [$F_{(2,205)} = 23.7$, $P < 0.0001$], TRI [$F_{(2,205)} = 17.9$, $P < 0.0001$], AD [$F_{(2,205)} = 6.4$, $P < 0.01$], and PD [$F_{(2,205)} = 6.8$, $P < 0.01$]. EMG responses for a representative subject illustrate that muscle activity was greatest when the stimulus was applied to digit V for all muscles, except for the PD (Fig. 5A). On average, withdrawal reflex responses were significantly greater when the stim-

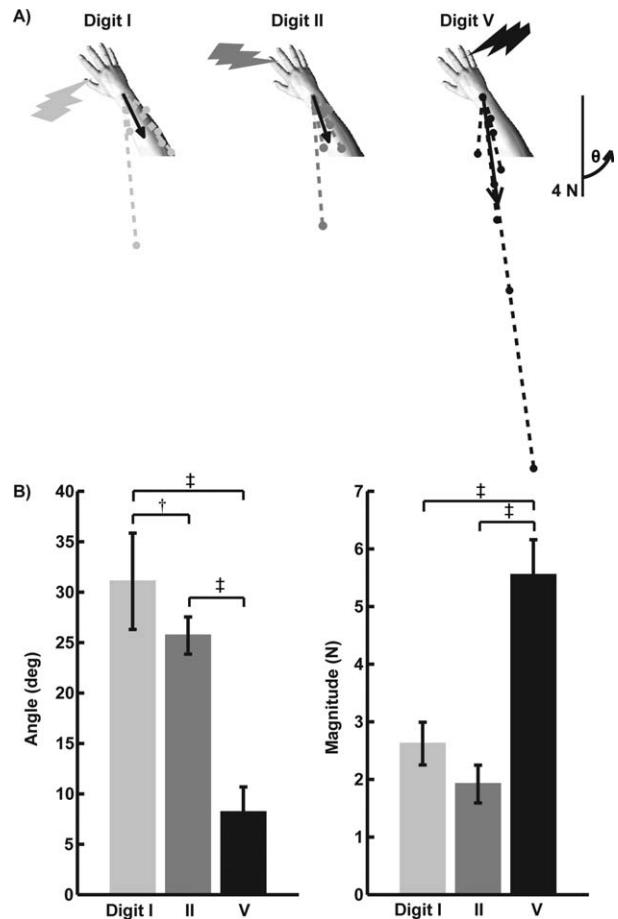


FIGURE 4. (A) Average force vectors across trials for each subject (dotted lines) and across subjects (black arrow) in each of the digit conditions. (B) Average force response angles (left) and magnitudes (right) across subjects in the 3 digit conditions with significant differences between digits denoted by † $P < 0.01$ and ‡ $P < 0.001$. Error bars are \pm standard error.

ulus was applied to digit V compared with digits I and II for all muscles, except for AD (difference between digits I and V not significant) and PD (Fig. 5B). For the PD, the EMG response when the stimulus was applied to digit I was significantly greater than the response when the stimulus was applied to digits II and V (Fig. 5B).

Response Latencies. Reflex responses were significantly faster than voluntary responses. The average latency for the force response (i.e., time from stimulus onset to force onset) elicited by nociceptive stimulation of digit II in the Middle posture was 103.5 ± 27 ms (average \pm SD; Table 1). This occurred at a significantly shorter latency than the initial force measured during voluntary withdrawal, which was 244.1 ± 41 ms [$F_{(1,116)} = 201.1$, $P < 0.001$]. Average latencies of the reflex EMGs (i.e., time from stimulus onset to EMG onset) in all muscles were also significantly smaller than the voluntary latencies (all $P < 0.001$; Table 1). Voluntary latency of the BIC and reflex latencies for the

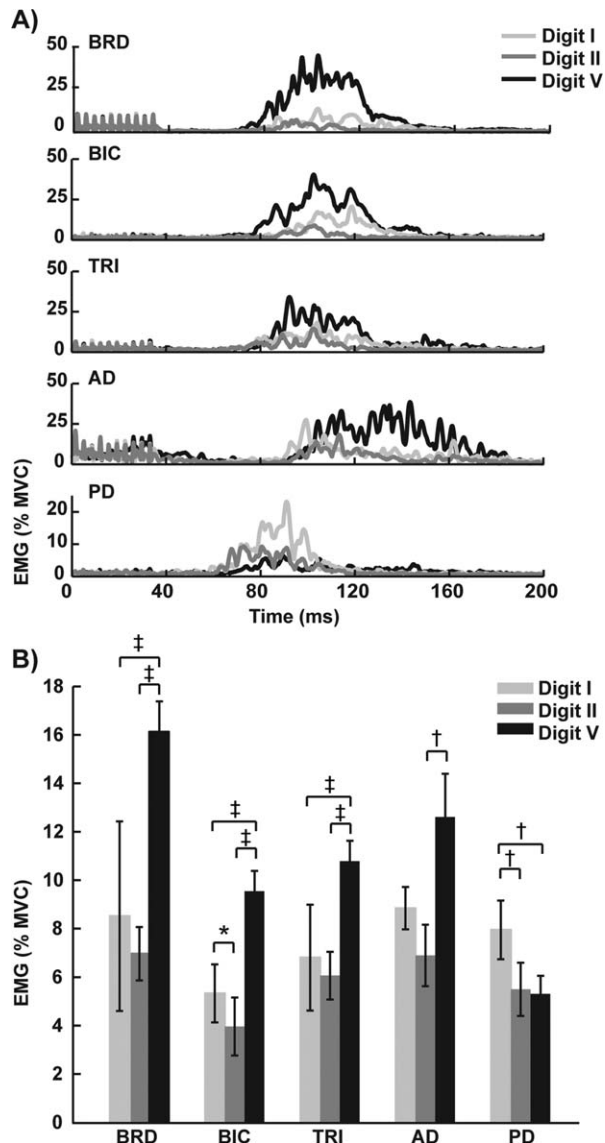


FIGURE 5. (A) Average EMG cross trials for a representative subject in the 3 digit conditions. (B) Average EMG reflex responses across subjects in the 3 digit conditions with significant differences between digits denoted by: * $P < 0.05$; † $P < 0.01$; and ‡ $P < 0.001$. Error bars are \pm standard error.

BIC and TRI correspond well to those reported by Floeter *et al.*,²⁷ who stimulated digit II using the same stimulus train as we did in this study. In

agreement with Dewald *et al.*,²⁸ the reflex latencies of the PD were shorter than those of the AD, and the latencies of the BRD and TRI were similar to the BIC. Also, the reflex force latencies in this study compare well to elbow and shoulder torque latencies reported previously.²⁸

Perceptual Thresholds. Perceptual thresholds (mean \pm standard deviation) in the Flexed, Middle, and Extended postures with digit II stimulation were 4.0 ± 1.0 mA, 3.7 ± 0.9 mA, and 3.8 ± 0.8 mA, respectively. Differences in subjects' perceptual threshold due to arm posture were not significant. Perceptual thresholds were 4.9 ± 1.1 mA, 3.7 ± 0.9 mA, and 3.9 ± 1.0 mA, with stimulation applied to digits I, II, and V in the middle posture, respectively. The digit stimulated had a small influence on the perceptual threshold, which was significantly greater with digit I stimulation compared with digit II [$F_{(2,27)} = 4.3$, $P = 0.024$]. Although constant nociceptive-stimulus intensity (above pain threshold) was used for each subject in each condition, the absence of any difference in magnitude of the reflex force response between digits I and II (Fig. 4B) suggests the use of a constant stimulus did not influence the results.

DISCUSSION

The purpose of this study was to determine whether withdrawal reflexes in the human upper limb, evoked by nociceptive electrical stimulation, adapt to different arm postures and stimulus locations (i.e., digits of the hand). We hypothesized that the withdrawal reflex would generate movement away from the stimulus, specific to the postural constraints on the limb and the digit stimulated. This hypothesis was supported by the consistent change in direction of the endpoint force initiated by the withdrawal reflex from a posterolateral direction to predominantly the posterior direction as the arm was moved from a flexed to a more extended posture, and also when the stimulus location was moved from digit I to V in a single posture. These results suggest that the

Table 1. Average and standard deviation (SD) of EMG and force latencies.*

Condition	Latencies (ms)					
	BRD	BIC	TRI	AD	PD	Force
Voluntary						
Middle, digit II	178.5 (31)	178.5 (38)	172.2 (41)	188.5 (72)	170.9 (45)	244.1 (41)
Reflex						
Middle, digit II	84.7 (16)	85.0 (15)	81.5 (11)	88.4 (12)	64.5 (17)	103.5 (18)
Flexed, digit II	84.5 (15)	83.3 (14)	71.9 (10)	85.8 (11)	65.3 (18)	109.3 (19)
Extended, digit II	90.6 (18)	86.5 (17)	84.2 (11)	86.6 (12)	68.1 (19)	104.3 (23)
Middle, digit I	78.6 (17)	80.5 (15)	76.6 (14)	82.7 (11)	66.8 (12)	109.0 (18)
Middle, digit V	79.0 (15)	77.5 (13)	81.6 (13)	87.2 (12)	75.5 (13)	106.6 (15)

*Data include time from stimulus onset to EMG and force onset, respectively, across subjects. Non-nociceptive stimuli were used for the voluntary trials.

withdrawal reflex in the upper limb can adapt to be relevant functionally in different conditions when it is elicited at rest in unimpaired subjects.

Posture-Dependent Withdrawal Reflexes. We expected that the direction of the withdrawal response would depend on arm posture. As a protective mechanism, the withdrawal reflex is only effective if it initiates motor actions that are appropriate for the configuration of the limb at the time of reflex activation. The posture-dependent shift in muscle activations and the corresponding direction of limb withdrawal suggests that there is some additional sensory input to the withdrawal reflex circuits encoding joint configuration. In particular, group II afferents have been shown to have a strong excitatory input to interneurons involved in the withdrawal reflex^{33,34} and, because group II afferents discharge continuously at static muscle lengths,³⁶ they are candidates for adapting to arm posture, although inputs from group Ia and cutaneous afferents may also contribute substantially.^{36,37}

A potential confound when interpreting the EMG results from the different arm postures is the likelihood that the relationship between the recording electrode and the muscle changed with posture. Although we cannot rule out the possibility that such movement introduced a posture-dependent effect in our data, it seems unlikely to account for the observed results. First, all muscles exhibited a similar trend of increasing activity at the more flexed postures, whereas posture-dependent changes due to relative movement of the recording electrode would more likely differ between agonists and antagonists acting at a single joint. Second, the EMG patterns were consistent with the endpoint forces, suggesting that there was indeed a posture-dependent change in the activation of the withdrawal reflex. Finally, our experiments evaluating the influence of stimulation location, described below, demonstrated the adaptability of the withdrawal reflex, even when the relationship between the recording electrodes and the muscles was fixed.

Digit-Dependent Withdrawal Reflexes. We also hypothesized that the motor action in the upper limb initiated by the withdrawal reflex would depend on which digit was stimulated. Consistent with previous reports from the lower limb that the reflex force response depends on the receptive field or nerve activated, the upper limb force response in this study was specific to the digit stimulated. The magnitude of the force response was greater when digit V was stimulated compared with digits I and II. The increased force response with digit V stimulation corresponded to increased muscle activity in all muscles except the PD. The increased BIC activ-

ity with digit V compared with digit II stimulation coincides with findings by Kofler *et al.*,²⁶ who found increased corticospinal facilitation of biceps brachii (i.e., greater motor evoked potential amplitude) when transcranial magnetic stimulation was preceded by noxious stimulation applied to digit V compared with digit II. We also found that TRI activity increased with digit V compared with digit II stimulation, although Kofler *et al.*²⁶ found no difference in triceps brachii facilitation between the digit conditions. Experimental differences in arm posture and fingertip stimulation (stimulus train vs. single pulse) between our study and Kofler *et al.*²⁶ warrant caution in these comparisons.

The digit-dependent responses are congruent with the activation of muscles appropriate to remove the limb from the noxious stimulus, as described previously in rats⁵⁻⁸ and the lower limb of humans.^{9,10} The change in the withdrawal reflex associated with the different stimulus locations was smaller in our study than previously reported in human lower limbs^{9,10} and was possibly limited by the restricted action at the wrist. Although the withdrawal response in the arm was specific to the digit stimulated, the motor action was always posterior or posterior-lateral. This general force direction may have been a limitation of the specific receptive fields that were examined or the use of ring electrodes rather than more focal stimuli, or it could suggest a difference in nociceptive spinal organization between the upper and lower limbs. Regardless, these results demonstrate that the withdrawal reflex in the upper limb is dependent on the location of the noxious stimulus.

EMG amplitudes and latencies of muscles supplied by the same myotome were not modulated in the same pattern and were not modulated according to the specific dermatome that was stimulated. For example, the PD was modulated differently based on the dermatome stimulated (digit I: C6; digit II: C7; digit V: C8) compared with the BRD, BIC, and AD (Fig. 5B), although these muscles are all supplied by the C5 myotome. Also, the TRI, which is supplied by the C7 myotome, was modulated in the same pattern as the BRD and BIC due to stimulus location (i.e., dermatomes). These results support a functional organization of withdrawal reflexes, as opposed to an organization according to myotomes innervated after stimulation of specific dermatomes, and coincide with data from Kofler *et al.*,²² who found the timing and magnitude of excitatory and inhibitory reflex EMGs differed in hand muscles supplied by the same myotome.

Functional Significance of Adaptable Withdrawal Reflexes. The posture- and digit-dependent changes in force and muscle activity suggest that

the withdrawal reflex can adapt to generate functionally appropriate responses that avoid a noxious stimulus. We elicited withdrawal reflexes from the arm at rest under isometric conditions in which it was possible to restrict voluntary activation of the motoneuron pools controlling the arm, thereby demonstrating modulation of the withdrawal reflex that was independent of background muscle activity as well as subsequent changes in muscle activity associated with proprioceptive feedback. These results add to the growing body of evidence demonstrating functional adaptation of the withdrawal response in the human arm. Earlier studies of withdrawal reflex adaptation in the upper limb have focused primarily on movement or suppression of muscle activity during voluntary contraction (cutaneous silent periods). Serrao *et al.*²¹ found that excitatory responses to nociceptive stimuli in upper limb muscles modulate with the phase (i.e., acceleration or deceleration) of movement during reach-grasp and grasp-lift tasks, whereas Don *et al.*¹⁹ reported that inhibitory responses adapt during movement by interrupting motion during reaching and by releasing an object during transport. Functional organization of protective inhibitory reflexes has been demonstrated by adaption of cutaneous silent periods to different stimulus locations in hand³⁸ and arm muscles²⁶ and adaptation to different elbow positions in the triceps brachii.²⁴ These observations, combined with the results of our study, suggest the excitatory and inhibitory components of the withdrawal reflex in the upper limb modulate relative to the stimulus location and limb posture to protect against injury.

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