



Deficits in startle-evoked arm movements increase with impairment following stroke



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HIGHLIGHTS

- Startle-evoked movements remain intact following stroke, but there are deficits specific to extension movements that increase with impairment level.
- These extension-related deficits appear to originate from a hypermetric classic startle reflex likely resulting from damage to cortical pathways.
- These results may have important implications for our understanding of deficits in stroke survivor's response to unexpected environmental disturbances.

ABSTRACT

Objective: The startle reflex elicits involuntary release of planned movements (startReact). Following stroke, startReact flexion movements are intact but startReact extension movements are impaired by task-inappropriate flexor activity impeding arm extension. Our objective was to quantify deficits in startReact elbow extension movements, particularly how these deficits are influenced by impairment.

Methods: Data were collected in 8 stroke survivors performing elbow extension following two non-startling acoustic stimuli representing “get ready” and “go”, respectively. Randomly, the “go” was replaced with a startling acoustic stimulus. We hypothesized that task-inappropriate flexor activity originates from unsuppressed classic startle reflex. We expected that increasing damage to the cortex (increasing impairment) would relate to increasing task-inappropriate flexor activity causing poor elbow extension movement and target acquisition.

Results: Task-inappropriate flexor activity increased with impairment resulting in larger flexion deflections away from the subjects' intended target corresponding to decreased target acquisition.

Conclusions: We conclude that the task-inappropriate flexor activity likely results from cortical or corticospinal damage leading to an unsuppressed or hypermetric classic startle reflex that interrupts startReact elbow extension.

Significance: Given startReact's functional role in compensation during environmental disturbances, our results may have important implications for our understanding deficits in stroke survivor's response to unexpected environmental disturbances.

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1. Introduction

A unique property of the startle reflex is its ability to involuntarily elicit pre-planned movements throughout the entire arm (Carlsen et al., 2004b, 2011; Honeycutt et al., 2013; Rothwell

et al., 2002; Valls-Solé et al., 2008, 1999). When a startling acoustic stimulus is presented in the absence of a movement plan, the classic startle reflex triggers brief co-contraction of muscles resulting in the individual assuming a protective stance – arm flexion in the upper limb. However, when a subject is in a state of movement preparation, a startling acoustic stimulus involuntarily elicits the prepared movement (Carlsen et al., 2004b; Rothwell et al., 2002; Valls-Solé et al., 1999; Valls-Solé, 1995). This phenomenon has been called startReact (Valls-Solé et al., 1999). Different from the classic startle response, startReact movements are not significantly

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different from voluntarily executed movements and reflect the sophistication of voluntarily planned movements in terms of acceleration and target accuracy (Carlsen et al., 2004a,b). While the classic startle response results in the generation of a protective, crouched posture, the startReact response appears to be more functionally relevant; specifically, it has been implicated in the ability to actively resist perturbations of the arm and whole-body. We recently demonstrated that arm perturbations, like startling acoustic stimuli, elicit startReact movements (Ravichandran et al., 2013) indicating that the functional role of this reflex likely participates in the effective and efficient response to an environmental perturbations. The startle reflex is also triggered during whole-body perturbations indicating startReact movements may also be functional during balance challenges (Blouin et al., 2006; Campbell et al., 2012; Oude Nijhuis et al., 2010; Siegmund et al., 2008).

The startReact phenomenon was recently shown to improve elbow flexion movements in stroke survivors (Honeycutt and Perreault, 2012) but startReact extension movements were impaired. While voluntary movements were slower with impaired muscle activity patterns, startReact elbow flexion movements were not statistically different from age-matched unimpaired individuals opening a discussion about its potential use in therapy. However, confounding results were found during elbow extension. While there was evidence that startReact extension movements were present, elbow extension was interrupted by task-inappropriate flexor activity causing either delay in elbow extension or elbow flexion away from a subject's intended target.

The specific mechanisms driving this inappropriate flexor activity are unknown making it challenging to properly develop startReact as a therapy tool. However, evaluating the impact of impairment level on task-inappropriate flexor activity following cortical stroke could shed some insight. Impairment level is linked to both lesion size and damage to the corticospinal tract (Ciccarelli et al., 2008; Mohr et al., 1993; Rogers et al., 1997; Saver et al., 1999; Zhu et al., 2010). By investigating changes in task-inappropriate flexor activity with impairment level, we can gain insight into the role of the cortex and the corticospinal tract in its expression. Therefore, our objective was to quantify deficits in startReact extension movements, particularly how these deficits are affected by impairment. These results will give insight not only to the mechanisms driving deficits in startReact extension but given startReact's functional role in responding to environmental perturbations, may also provide key insights into the mechanisms driving a stroke survivor's impaired responses to arm and balance perturbations.

We have previously hypothesized that the task-inappropriate flexor activity originates from unsuppressed classic startle reflex. This hypothesis was driven by the knowledge that the (1) classic startle response is dominated by flexor activity, (2) amplitude of the classic startle response is modulated by the cortex (Alibiglou and MacKinnon, 2012; Davis et al., 1982; Davis and Gendelman, 1977; Groves et al., 1974), and (3) the classic startle reflex is hypermetric or enlarged following stroke (Jankelowitz and Colebatch, 2004). Damage to the cortex following cortical stroke should diminish the capacity of the cortex to suppress the classic startle reflex during startReact movements. Therefore, we expect that increasing damage to the cortex (increasing impairment) will result in increasing task-inappropriate flexor activity corresponding to increasing deficits in elbow extension movement and decreasing target acquisition. Further, as classic startle is known to adapt (diminish in amplitude over time), we expect that the task-inappropriate flexor activity will diminish over time leading to increasingly appropriate elbow extension movement. A correct hypothesis would indicate that the task-inappropriate flexor activity likely arises from unsuppressed classic startle. Functionally, this

result would highlight that more severely impaired individuals will have increased movement trajectory errors that move then away from their intended extension targets during external disturbances.

2. Methods

2.1. Subjects

Data were collected from 8 chronic stroke subjects ranging in age from 47–81 (mean: 68 ± 9.8) (Table 1). Stroke subjects with a range of impairment levels were recruited. Impairment was assessed using the upper extremity Fugl-Meyer (UEFM) score, which ranged from 12 to 59. Inclusion criteria for the stroke subjects included: a unilateral cortical brain lesion from a stroke at least one year prior to the study, an ability to understand the task, lack of aphasia, and a stroke that affected the arm that was dominant prior to injury. We evaluated the dominant arm of all subjects as startReact movements have been studied largely in the dominant arm (Carlsen et al., 2011). All protocols and recruitment procedures were approved by Northwestern's Institutional Review Board (IRB).

2.2. Equipment

In all experiments, the arm was positioned at approximately 70 degrees of shoulder abduction and 25 degrees shoulder flexion; the elbow was positioned at 90 degrees. All subjects were fitted with a custom-made thermoplastic cast that immobilized the wrist and held the arm in the prone position. The top of cast was attached to a force sensor (45E15A4; JR3 Inc, Woodland, CA), which was coupled to a one degree of freedom rotary motor (BSM90N; Baldor Electric Company, WV) through a 10:1 planetary gear (AD140-010-PO; Apex Dynamics, Taiwan). The center of rotation was fixed just above the elbow joint. The rotary motor was used to ensure a repeatable and measured trajectory for evaluation of muscle activity patterns and position, and to support the weight of the arm against gravity. The rotary motor did not assist or perturb the elbow in any way. Rather, it was configured as an admittance controller set to mimic the properties of a passive inertial load ($0.2 \text{ kg-m}^2/\text{rad}$) in the flexion/extension axis.

Bipolar Ag/AgCl electromyography (EMG) electrodes (Noraxon Dual Electrodes, #272, Noraxon USA Inc., AZ) were used to record muscle activity from the brachioradialis (Br), triceps long head (TriLo), and the left and right sternocleidomastoid (SCM) muscles. EMG signals were amplified and conditioned using a Bortec AMT-8 (Bortec Biomedical Ltd., Canada), with a band-pass filter of 10–1000 Hz. The resulting signals were anti-alias filtered using 5th order Bessel filters with a 500 Hz cut-off frequency and sampled at 2500 Hz (PCI-DAS1602/16; Measurement Computing, MA). Elbow position was recorded by an encoder with an effective resolution of 0.0036 degrees. EMG and position data were sampled

Table 1
Subject characteristics.

| Subject # | Sex | Age | Paretic Limb* | Years since Stroke | UEFM | Chedoke Arm |
|-----------|-----|-----|---------------|--------------------|------|-------------|
| 1 | M | 68 | L | 10 | 34 | 4 |
| 2 | M | 81 | R | 17 | 24 | 3 |
| 3 | M | 61 | R | 8 | 54 | 5 |
| 4 | F | 70 | R | 22 | 40 | 4 |
| 5 | M | 69 | R | 6 | 12 | 2 |
| 6 | M | 74 | R | 23 | 15 | - |
| 7 | M | 65 | R | 11 | 22 | 3 |
| 8 | M | 47 | R | 36 | 59 | 5 |

*Paretic limb was dominant hand prior to stroke.

-Scores were not available.

synchronously. All data collection was synchronized to the GO signal using a pre-trigger collection time of 1 s and post-trigger collection time of 5 s.

2.3. Protocol

Each subject was trained to perform ballistic elbow extension movements of 25 degrees. A computer screen displayed two circles: HOME (located centrally) and TARGET (located at 25 degrees elbow extension). Subjects were instructed to move into the HOME circle and wait for two non-startling (80 dB) auditory cues. The first cue (WARNING) signaled the start of the trial, and indicated that the subject should prepare to move. The second cue (GO) was the prompt to initiate the intended movement as rapidly as possible. The GO occurred randomly 2.2–2.5 s following the WARNING. Subjects were asked to move as quickly as possible from the HOME to TARGET circle. Subjects were instructed to reach to the target as fast as possible. They were given 2–3 s to complete the task, but no specific instructions were provided with respect to accuracy. A successful reach was defined as one that exceeded the 25 degree target on the first attempt. Subjects were first trained in the task until they responded reliably and consistently to the GO signal; this typically occurred after approximately 30 trials. After training, a startling auditory stimulus of 128 dB was randomly delivered in place of the GO. During a block of 15 trials, startling acoustic stimuli were randomly delivered 3–4 times at the GO. Subjects performed between 2–3 blocks resulting in 6–8 startReact trials collected in each subject. Subjects were given no instruction on how to respond to the startling acoustic stimulus.

2.4. Data analysis

Position and EMG traces were visually inspected to eliminate trials in which the subject moved out of HOME prior to the GO or any especially slow trials in which subjects did not move at the GO. Next, SCM muscle activity was evaluated in all trials (voluntary and startReact). Activity in the SCM muscle is known to indicate the presence of startle (Carlsen et al., 2011; Valls-Solé et al., 1999). We considered activity in either the left or right SCM muscles within 120 ms of the acoustic stimulus to indicate the presence of startle (Blumenthal et al., 2005). Using this criterion, all trials with SCM activity present in either left or right SCM were classified as SCM+ (startle occurred). Those without SCM activity were classified as SCM– (startle was not detected). Only SCM– voluntary reaching trials and SCM+ startReact reaching trials were analyzed further, which yielded an inclusion rate of 89% voluntary reach and 80% startReact trials in stroke subjects. As SCM+ voluntary reaching trials were elicited during a different acoustic-intensity, which can impact onset latency (Kohfeld, 1969), these trials were excluded from analysis of SCM+ trials.

The latency of muscle activity onset was calculated from the rectified EMG recorded in each trial. The average background activity and standard deviation prior to the stimulus were calculated. Next an automated program identified the time at which the processed EMG increased above 2.5 times the standard deviation of the background activity for a period of 15 ms. Following the automatic detection of EMG onset, each trial was evaluated visually to ensure accuracy. The amplitude of the EMG was computed as the average rectified response for a window of 70 ms following the detected onset. A previously reported impairment during startReact extension movements following stroke is abnormal elbow flexion activity prior to the planned extension movement. This was quantified by the maximum elbow flexion during the planned elbow extension trials. In addition in order to quantify the time course of the observed trajectory, the elbow position was calculated at 150, 300, and 450 ms following movement initiation. The subject's

ability to reach the intended target was quantified as the trials in which the 25 degree target was reached on the first attempt and was represented as a probability.

2.5. Statistical analysis

First, we quantified the startReact response in comparison to voluntary movement. Muscle onset latency was compared between voluntary and startReact trials. An ANOVA was completed using a linear mixed-effect model. Muscle onset latency was treated as the dependent variable, while trial type (voluntary vs startReact) and muscle type (Br and TriLo) were treated as the independent variables. Subjects were treated as a random effect and a Tukey post hoc test, which corrects for multiple comparisons, utilized. Our first hypothesis was that increasing damage to the cortex (increasing impairment) would relate to an increase in task-inappropriate flexor activity and consequently to increasing deficits in elbow extension movement and target acquisition. In order to assess the impact of impairment on the inappropriate flexor activity and resulting target acquisition, a linear regression was performed at a confidence interval of 95% with impairment (Upper-Extremity Fugl-Meyer or UEFM score) as the independent variable and the maximum elbow flexion deflection, startReact target acquisition, and average muscle onset latency as the dependent variables. Our second hypothesis was that the task-inappropriate flexor activity would diminish over time leading to increasingly appropriate elbow extension movement over time. In order to assess if the flexor activity diminished in amplitude over time, an ANOVA was performed with elbow position at three time points (150, 300, 450 ms), EMG amplitude, and EMG latency as the dependent variables and trial number as the independent variable. Subjects were treated as random effects and trial number was treated as a continuous variable.

3. Results

Task-inappropriate flexor activity influenced startReact extension movements across all impairment levels (Fig. 1). Appropriate agonist (TriLo) activity preceding antagonist (BR) activity was present during voluntary elbow extension movements (gray). However during startReact elbow extension movements (black) the antagonist BR muscle activity preceded or occurred at the same latency as agonist BR activation. This was confirmed by group results. Onset latency was influenced by trial type ($F_{1,368} = 379$; $p < 0.0001$) and muscle type ($F_{1,368} = 195$; $p < 0.0001$) with a significant interaction ($F_{1,368} = 80$; $p < 0.0001$). Therefore, the average onset latency of the TriLo (211 ± 110 ms) and Br (387 ± 147 ms) muscles during voluntary movements was different ($p \approx 0$), while the onset latencies of TriLo (98 ± 33 ms) and BR (83 ± 23 ms) were not different during startReact extension ($p = 0.25$).

While task-inappropriate flexor activity was present in all subjects evaluated, it led to the most significant deviation from the extension target in more severely impaired individuals. Individuals with mild impairment (Fig. 1A) demonstrated a delay in elbow movement towards extension, while individuals with moderate and severe impairment demonstrated large elbow flexion movements prior to elbow extension (Fig. 1B and C). Quantification of group results established that maximum elbow flexion deflection and startReact extension target acquisition were related to impairment level. Maximum elbow flexion deflection (Fig. 2A: $p = 0.016$) increased with increasing impairment (decreasing UEFM). Similarly, the probability of startReact extension movements reaching the target (Fig. 2B: $p = 0.0009$) decreased with increasing impairment, even though the probability of reaching the extension target during voluntary movements was not related to impairment

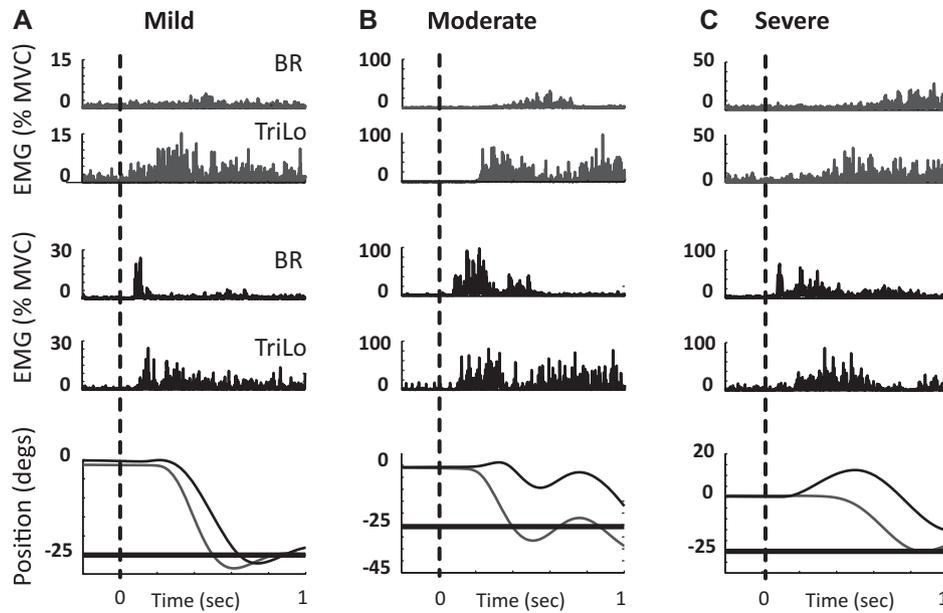


Fig. 1. EMG responses from the BR and TriLo muscles and elbow position during voluntary (gray) and startReact (black) trials. (A) Mild impairment, UEFM = 56 (B) Moderate impairment, UEFM = 34 (C) Severe impairment, UEFM = 15. Black line indicates extension target.

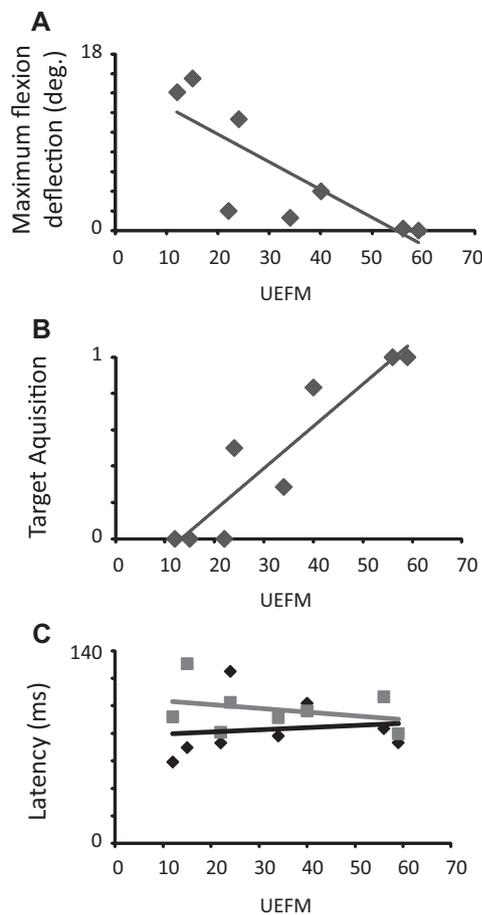


Fig. 2. Quantification of startReact deficits across impairment level. (A) The maximum flexion deflection position during startReact trials for each subject graphed against Upper Extremity Fugl-Meyer (UEFM) scores. (B) The probability of target acquisition during startReact trials graphed against UEFM. (C) Onset latency for BR (black) and TriLo (gray) muscles against impairment.

($p = 0.12$). Still, changes in elbow flexion deflection and target acquisition were not related to changes in muscle onset latency.

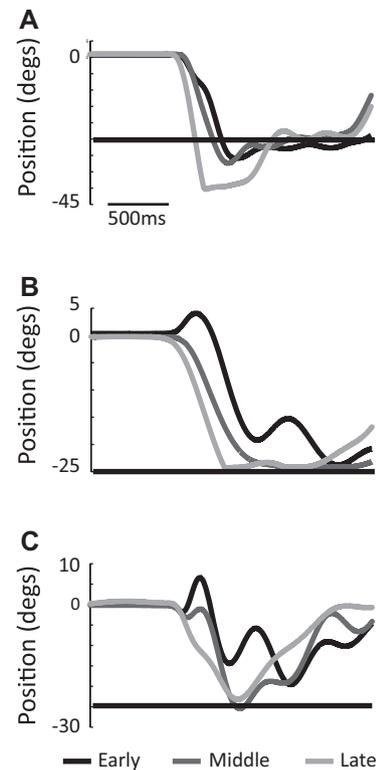


Fig. 3. Elbow position presented across early, middle, and late startReact trials to depict changes in elbow position over time. (A) Mild impairment, UEFM = 59 (B) Moderate impairment: UEFM = 40. (C) Severe impairment: UEFM = 24. Black line represents extension target.

BR ($p = 0.79$) and TriLo ($p = 0.47$) muscle onset latencies were not related to changes in impairment (Fig. 2C).

Regardless of impairment, elbow position showed decreasing movement in the flexion direction in successive trials (Fig. 3) and coincided with decreasing BR muscle amplitude (Fig. 4). All subjects showed improved startReact extension movements over time. In mild impairment, the inappropriate flexor activity led to a delay of movement in the extension direction that dissipated in

subsequent trials leading to faster target acquisition (Fig. 3A). Moderately and severely impaired individuals showed movement trajectories that did not deflect towards flexion in later trials. Group results confirmed that improvements in elbow trajectory were seen in all subjects. Specifically while elbow position was not affected by trial number at 150 ms ($F_{(1,46)} = 0.97$; $p = 0.34$), it was affected at 300 ms ($F_{(1,46)} = 8.52$; $p = 0.006$) and 450 ms ($F_{(1,46)} = 22.6$; $p = 0.0001$) (Fig. 4A). Improvements in elbow position trajectory were accompanied by decreased BR muscle amplitude, which was influenced trial number ($F_{(1,43)} = 13.3$; $p = 0.0021$). Conversely, TriLo muscle amplitude remained constant ($F_{(1,43)} = 0$; $p = 0.99$) (Fig. 3B) indicating that changes in elbow position were related to changes in BR muscle amplitude. While the amplitude of the BR muscle activity was diminished, the onset

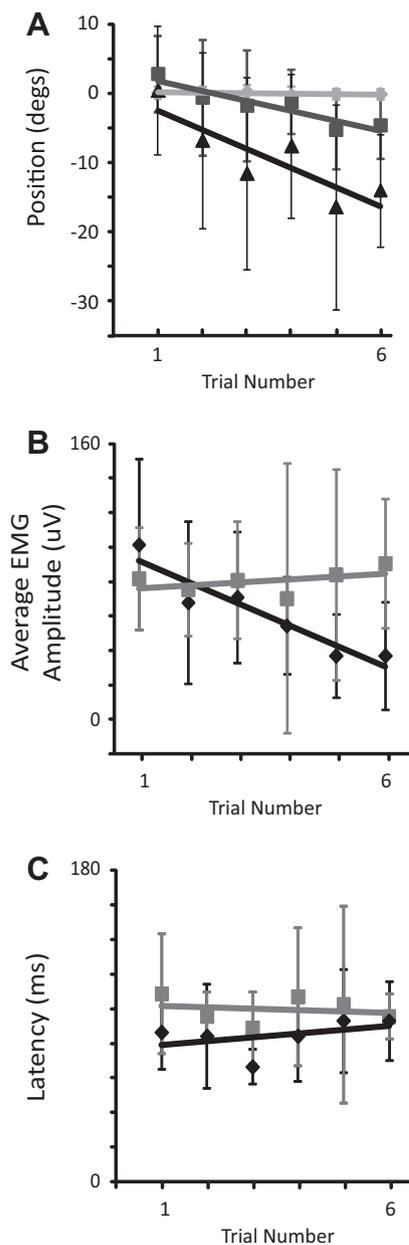


Fig. 4. Change in position, EMG amplitude, and onset latency over successive trials. (A) Arm position during startReact at 150 ms (light gray), 300 ms (dark gray), and 450 ms (black) across trials. (B) Average EMG amplitude during startReact for the BR (black) and TriLo (gray) muscles across trials. (C) Onset latencies during startReact for the BR (black) and TriLo (gray) muscles across trials.

latency of BR ($F_{(1,42)} \approx 0$; $p = 0.98$) and TriLo ($F_{(1,45)} \approx 0$; $p = 0.96$) were not impacted by trial number (Fig. 3C) indicating that while the task-inappropriate flexor activity diminished, it was not eliminated over the course of the experiment.

4. Discussion

We hypothesized that the task-inappropriate flexor activity during startReact elbow extension originates from unsuppressed classic startle reflex. Therefore, we expected that (1) increasing damage to the cortex (increasing impairment) would relate to an increase in task-inappropriate flexor activity and consequently to increasing deficits in elbow extension movement and target acquisition and (2) that task-inappropriate flexor activity would diminish over time leading to increasingly appropriate elbow extension movement over time. We indeed found that task-inappropriate flexor activity increased with impairment leading to larger elbow flexion deflections away from the subjects' intended extension target and corresponded to decreased target acquisition. Moreover, severely impaired individuals UEFM <25 never achieved the extension target during startReact trials. While this task-inappropriate flexor activity diminished leading to improved elbow trajectories over subsequent trials, the inappropriate activity was not eliminated over the course of these experiments. As functional motor impairment is linked to both cortical lesion size (Mohr et al., 1993; Rogers et al., 1997; Saver et al., 1999) and damage to the corticospinal tract (Ciccarelli et al., 2008; Zhu et al., 2010), the task-inappropriate flexor activity is likely driven by damage to the cortex or corticospinal tract. Interestingly, adaptation (or diminishing of the flexor activity over time) remained intact in all impairment levels suggesting it is mediated by alternative neural pathways. Finally, as startReact responses are triggered during perturbations of the arm and whole-body, more severely impaired individuals likely will have increased movement trajectory errors that specifically move then away from their intended extension targets during external disturbances.

4.1. Mechanisms driving deficits in startReact following stroke

There is growing evidence that classic startle and startReact are separate phenomena mediated by overlapping but distinctive neural structures (Alibiglou and MacKinnon, 2012; Kumru et al., 2006; Maslovat et al., 2012). In unimpaired individuals, classic startle results in brief, synchronous activity of upper limb muscles which is dominated by flexion (Brown et al., 1991). During startReact movements, a startling stimulus releases a planned movement that is not different in muscle activation patterns and target accuracy from a voluntarily elicited planned movement (Carlsen et al., 2011; Maslovat et al., 2011; Valls-Solé et al., 1999; Valls-Solé, 1995). In unimpaired individuals, only the planned movement is elicited and the classic startle response is not quantitatively observed in the upper limb muscles (Carlsen et al., 2011). Animal work demonstrated that the cortex modulates the amplitude of the classic startle reflex (Davis and Gendelman, 1977). Similar results occur in humans as cortical damage leads to hypermetric classic startle responses (Jankelowitz and Colebatch, 2004; Rothwell, 2006). Therefore following a stroke, it is probable that cortical damage impairs the ability to suppress the classic startle reflex during startReact leading to a simultaneous release of both classic startle and startReact. This phenomenon has been observed in other subcortical reflexes e.g. hypermetric stretch reflexes or spasticity (Krakauer, 2005; Levin, 1996; Zackowski, 2004) and a resurgence of the typically dormant asymmetric tonic neck reflexes following stroke (Ellis et al., 2012; Lee et al., 2009; Yamshon et al., 1949). Further, the task-inappropriate flexor

activity shares several common features with the classic startle reflex. The task-inappropriate flexor activity shows adaptation over time which has been observed in classic startle (Valls-Solé et al., 1997) but not startReact (Carlsen et al., 2011). Further the task-inappropriate flexor activity is not statistically different in onset latency from the agonist (TriLo) muscle, which also closely resembles the synchronous agonist/antagonist firing of the classic startle reflex. These observations suggest that the task-inappropriate flexor activity is the result of unsuppressed or hypermetric classic startle resulting from cortical damage.

It is important to note that an intact startReact extension movement is likely present. First, there is a significant decrease in onset latency in the agonist, TriLo muscle during startReact extension (98 ms) from voluntary (211 ms). TriLo muscle activation showed consistent activation over the duration of the experiment, distinctive from the diminishing activity in the BR muscle, indicating that the mechanisms driving BR and TriLo muscle activation are distinctive. Second, startReact extension resulted in elbow extension. If the classic startle was the only response, we would expect to see only movement in the flexion direction (Brown et al., 1991; Honeycutt and Perreault, 2012; Jankelowitz and Colebatch, 2004; Yeomans and Frankland, 1996). Finally, we have previously reported that startReact elbow flexion movements are intact and statistically indistinguishable from neurologically healthy age-matched individuals. (Honeycutt and Perreault, 2012) indicating that when task-inappropriate flexor activity does not interrupt movement an appropriate movement can be elicited. This is particularly interesting given that voluntary executed elbow flexion movements are significantly impaired in stroke survivors in comparison to neurologically healthy individuals. startReact elbow flexion movements are likely not impaired by the unsuppressed startle because this activity assists the flexion movement while it opposes elbow extension. Therefore, we conclude that the task-inappropriate flexor muscle activation most likely results from unsuppressed classic startle.

An alternative mechanism that could drive the task-inappropriate flexor activity is spasticity that often leads to tonic co-contraction during movement in stroke survivors (Dietz and Sinkjaer, 2007; Dietz et al., 1991; Krakauer, 2005; Levin, 1996). However, this is not a probable explanation as spasticity occurs in the response to stretch and the onset latency of the BR muscle is concurrent with the TriLo muscle indicating that it does not result from stretch initiated during movement. Further, the BR activity diminishes in amplitude which would be unexpected if the cause was spasticity.

4.2. Functional consequences

The ability to quickly and effectively compensate during environmental perturbations is essential to everyday tasks and injury prevention. It is well-established that following stroke individuals have important deficits resisting perturbations of the arm and ankle (Dietz and Berger, 1984; Dietz et al., 1991; Finley et al., 2008; Lum et al., 2004; Sangani et al., 2007; Trumbower et al., 2013, 2010). Perturbation-specific, short and long latency stretch reflexes, are significantly impaired following stroke disrupting their ability to resist arm perturbation (Dietz and Berger, 1984; Dietz et al., 1991; Lum et al., 2004; Trumbower et al., 2013, 2010) leading to a reduced torque capacity. Recent evidence demonstrates that this ability is driven not only by perturbation-specific stretch reflexes but also by task-specific early release of planned movement (Hammond, 1956; Lewis et al., 2006; Ravichandran et al., 2013). startReact movements are identical in complexity and muscle activation patterns as voluntarily planned movements but they are elicited 30–40 ms faster – a time that overlaps with the long-latency stretch response to environmental perturbations (Crago

et al., 1976; Gottlieb and Agarwal, 1979). Recent work from our laboratory demonstrates that startReact movements are triggered during perturbations of the arm (Ravichandran et al., 2013). When startReact is not present, the subject has a significantly diminished and delayed reaction to perturbation indicating that this reflex plays an important role in quickly and effectively resisting perturbations of the arm (Smith et al., 2011).

Furthermore, our results demonstrate that more severely impaired individuals have more severe deficits in startReact extension. Thus, more severely impaired individuals will have increased movement trajectory errors that move them away from their intended extension targets during external disturbances. When coupled with the decreased muscle strength, spasticity, and loss of functional control over the limb, places these individuals at significant risk of injury.

While the role of startReact during whole-body perturbations remains less certain, startle has been recorded during perturbations of the whole body. Furthermore, the startle reflex is mediated in part by the brainstem (Davis et al., 1982; Groves et al., 1974; Hammond, 1973; Rothwell, 2006; Yeomans and Frankland, 1996), which has known importance during corrective responses during balance challenges (Deliagina et al., 2008; Honeycutt et al., 2009; Honeycutt and Nichols, 2010; Mori, 1987; Mori et al., 1989; Musienko et al., 2008; Schepens et al., 2008; Stapley and Drew, 2009). Thus, it is possible that task-inappropriate flexor activity could lead to movement away from a subject's intended target during balance challenges. Further research is needed to establish a link between the deficits described here and those that occur during active resistance of environmental perturbations.

4.3. Limitations

Our results are limited by a lack of detailed lesion data. More thorough imaging data could provide important information about the role of the cortex in these types of responses. Furthermore, tractography (imaging technique quantifying impairment to neural tracts) of the corticospinal tract would provide more definitive evidence that the task-inappropriate flexor activity results from damage of this neural tract.

Finally in this study the arm is supported against gravity and movement restricted to the elbow. Therefore in more functional and less restricted situations, the impact of task-inappropriate flexor activity may be more significant. Furthermore, spasticity and abnormal muscle activation patterns (synergies) would likely also more significantly disrupt movement during these conditions.

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