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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.

1. Introduction

A unique property of the startle reflex is its ability to involuntary 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 kg-m^2/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.