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Instruction-dependent modulation of the long-latency stretch reflex is associated with indicators of startle

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Abstract

Long-latency responses elicited by postural perturbation are modulated by how a subject is instructed to respond to the perturbation, yet the neural pathways responsible for this modulation remain unclear. The goal of this study was to determine if instruction-dependent modulation is associated with activity in brainstem pathways contributing to startle. Our hypothesis was that elbow perturbations can evoke startle, indicated by activity in the sternocleidomastoid muscle (SCM). Perturbation responses were compared to those elicited by a loud acoustic stimulus, known to elicit startle. Postural perturbations and startling acoustic stimuli both evoked SCM activity, but only when a ballistic elbow extension movement was planned. Both stimuli triggered SCM activity with the same probability. When SCM activity was present, there was an associated early onset of triceps EMG, as required for the planned movement. This early EMG onset occurred at a time often attributed to long-latency stretch reflexes (75-100ms). The nature of the perturbation-triggered EMG (excitatory or inhibitory) was independent of the perturbation direction (flexion or extension) indicating that it was not a feedback response appropriate for returning the limb to its original position. The net EMG response to perturbations delivered after a movement had been planned could be explained as the sum of a stretch reflex opposing the perturbation and a startle-evoked response associated with the prepared movement. These results demonstrate that rapid perturbations can trigger early release of a planned ballistic movement, and that this release is associated with activity in the brainstem pathways contributing to startle reflexes.

Keywords

stretch reflex; triggered reaction; long latency reflex; startle

Introduction

The earliest involuntary response to perturbations of upper limb posture, the stretch reflex, consists of a short-latency response occurring 20-50 ms after perturbation onset. The properties and mechanisms of this reflex have been described well (Burke et al., 1984;

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Liddell and Sherrington, 1924; Lloyd, 1943); however, the properties and mechanisms of the longer latency stretch response, occurring 50-100 ms after perturbation onset, remain less understood. Previous research has suggested two potential roles for the long-latency reflex in the control of posture and movement. It has been proposed that this reflex contributes to the maintenance of limb stability by *resisting* imposed limb perturbations in a manner appropriate for the mechanics of the task environment and the limb (Doemges and Rack, 1992; Dietz et al., 1994; Perreault et al., 2008; Krutky et al., 2010; Krutzy et al., 2008; Pruszynski et al. 2011b). There is also evidence that perturbation-elicited responses within this time period are related to prepared movement plans, *assisting or resisting* limb perturbations according to the planned action (Hammond, 1956; Colebatch et al., 1979; MacKinnon et al., 2000; Lewis et al., 2006). While the component of the long-latency response associated with maintaining arm stability appears to at least partially involve the cortex (Kimura et al., 2006; Shemmell et al., 2009; Pruszynski et al. 2011a), the component associated with planned motor actions may reflect the early release of those actions, hastened by the perturbation applied to the limb (Crago et al., 1976; Koshland and Hasan, 2000), and may therefore assist or resist the perturbation. The neural elements responsible movement-related component of the long-latency stretch reflex are not yet known, although it appears to be less dependent on the primary motor cortex (Shemmell et al., 2009). Identifying the mechanisms driving responses elicited during movement preparation would clarify the role of the stretch reflex in the control of posture and movement.

It is well established that planned motor actions of the upper limb can be released early by a startling acoustic stimulus (Valls-Solé et al., 1999; Carlsen et al., 2004). The earliest muscle activation triggered by startling auditory stimuli occurs at ~70-80 ms, within the range ascribed to the long-latency stretch reflex and much earlier than the onset of most voluntary actions. Muscular responses to startling acoustic stimuli appear to be mediated by neurons within the pontine reticular formation of the brainstem since lesions in this area prevent startle responses (Yeomans et al, 1999; Lingenhöhl and Friauf, 1994); for review see Yeomans, 2002). The involvement of brainstem circuits in the transmission of auditory startle responses is also supported by intracellular recordings showing activation of pontine reticular formation neurons at short-latency following high-intensity acoustic stimulation (Lingenhöhl and Friauf, 1994). In humans, activation of sternocleidomastoid muscle (SCM) has been used to identify a startle response (Carlsen et al., 2003). By monitoring SCM activity it is therefore possible to identify muscular responses that involve activation of startle response circuits in the brainstem.

The purpose of this study was to determine if the activation of startle response circuits is a contributor to the task-specific modulation of stretch reflex amplitude observed when the arm is perturbed after a ballistic movement has been fully prepared. We hypothesized that perturbation of the elbow joint would activate the SCM, an indicator of startle circuit activation, only in the presence of a movement plan, and that this activity would coincide with the early release of the planned movement. We also directly compared muscle activity elicited by a mechanical perturbation of the arm to that elicited by a startling acoustic stimulus, hypothesizing that both would result in activation of the SCM, and a similar early release of the planned movement.

Methods

Participants

Ten right-handed, able-bodied individuals (age: 27 ± 3 , 6 females and 4 males) with no known neurological disorders volunteered to participate in the experiment. The right arm was used for testing for all participants. All protocols were approved by the Northwestern

University Institutional Review Board (IRB Protocol STU00009204) and required informed written consent.

Equipment

Participants were seated comfortably with the trunk secured to an adjustable chair (Biodex, NY) using padded straps such that their initial posture was at 70° shoulder abduction, 0° shoulder flexion, and the elbow was at 90° flexion. This was the HOME position for all trials types (see Protocol). The wrist was immobilized in a neutral position using a rigid custom-made plastic cast (Fig. 1). The cast was directly attached to a force sensor (45E15A4-I63-AF 630N80; JR3 Inc, Woodland, CA) mounted on a rotary motor (BSM90N-3150, Baldor Electric Company, WV), aligned such that the motor axis was in line with the elbow flexion/extension axis. The rotary motor was attached to a 10:1 planetary gear head (AD140-010-PO; Apex Dynamics, Taiwan ROC). Motor rotation was measured by an encoder with a resolution of 0.036 degrees, resulting in a measurement resolution of 0.0036 degrees for the elbow displacements, due to the influence of the gear ratio.

The rotary motor was configured as an admittance servo, allowing us to simulate both rigid (stiffness = 30000 Nm/rad) and compliant (stiffness = 0 Nm/rad) environments. For both environments, the moment of inertia was set to 0.2 kgm²/rad and a critical damping was used. The rigid configuration was used during the application of perturbations and the compliant configuration was used during voluntary movements. Physical stops limited the actuator to 20° of flexion and 45° of extension relative to the nominal elbow position. Software limits were implemented to prevent motion 10° before contact with the physical limits. To ensure participant safety, both the participant and the experimenter were provided with their own respective stop buttons that cut power to the motor.

Surface electromyographic (EMG) activity was recorded from the lateral head of the triceps brachii, and the left sternocleidomastoid (SCM) using bipolar Ag/AgCl electrodes (Noraxon Dual Electrodes, #272, Noraxon USA Inc., AZ). EMGs were amplified and conditioned using a Bortec AMT-8 (Bortec Biomedical Ltd., Canada), with a band-pass filter of 10-1,000 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 using an Analog to Digital converter (PCI-DAS1602/16; Measurement Computing, MA). Visual feedback of the current elbow angle was provided on a computer monitor placed directly in front of the participant (Fig. 1).

Two types of auditory signal were used. The first was non-startling tone of 80dB presented via a Sonalert SC628ND speaker (Mallory Sonalert Products Inc., IN) mounted on the monitor used for visual feedback. The second was a startling stimulus of 118 dB presented using a piezo-dynamic siren (M85PDS; MG Electronics, NY) placed 20 cm directly behind the head of the participant. The intensity of the startling stimulus was measured using a digital sound level meter (Model 407730, Extech Instruments Corp, MA). The duration of all auditory signals was limited to 40 ms.

Protocols

Our experiments were designed to determine if elbow perturbations elicit a startle-like response in the triceps, when participants have prepared but not yet executed an elbow extension movement. This was accomplished by comparing activity in the triceps and sternocleidomastoid muscles elicited by elbow perturbations to the same activity when elicited by startling acoustic stimuli.

A series of isometric maximum voluntary contractions (MVCs) were performed at the start of the experiment, while the participant was held rigidly by the motor. Each muscle

contraction lasted for approximately 3 seconds. These data were used to normalize the EMGs recorded from each muscle.

The main experiment consisted of a *posture-maintenance* phase, a *movement-training* phase, and a *movement-testing* phase. In all phases the rotary motor was set to simulate a compliant environment (stiffness = 0 Nm/rad) with a bias torque of 2Nm in the flexion direction. This bias torque was used in an effort to control the input to the triceps motoneuron pool, thereby reducing the variability in the elicited reflex responses.

The posture-maintenance phase was used to obtain reflex responses in the absence of any prepared movement plan. Participants were instructed to move into the HOME position, defined as 90° of elbow flexion, and to “do not intervene” (DNI) with the applied perturbation. Perturbations were applied after the HOME position ($\pm 1^\circ$) had been held for a randomized duration of time lasting between 0.5-1.0 s. Twenty perturbations were randomly applied in both the flexion (DNI:FLEX) or the extension (DNI:EXT) directions (Fig 2); the order of randomization was varied trial-by-trial and across participants.

In the movement-training phase, participants were trained to perform 40 ballistic movements from the HOME position to a target located 25° away in the extension direction (Figure 1). Two non-startling, 80 dB auditory cues were presented. Participants were instructed to treat the first cue as a WARNING (prepare to move) and the second as a GO (move to target). The WARNING cue was provided after the participants had held the HOME position ($\pm 1^\circ$) for a random duration between 0.5 – 1s. A randomized time interval of 2.5 – 3.5s after the WARNING, the GO cue was delivered. Randomization was utilized to ensure participants could not predict the GO cue. Participants were instructed to move to the target as soon as possible. Trials from the movement-training phase were not used for subsequent data analysis.

The movement-testing phase was identical to the movement-training phase, except that *probe* trials were randomly applied to assess reflex responses. Participants completed 180 voluntary movement trials (MOV:VOL), split into 5 blocks of 36 trials each. Thirty random, non- consecutive probe trials (Figure 2) were interspersed throughout these blocks. In these probe trials, the GO signal was presented concomitantly with one of the following stimuli: a startling acoustic stimulus (MOV:SAS) of 118dB, an elbow extension perturbation (MOV:EXT), or an elbow flexion perturbation (MOV:FLEX). The ramp-and-hold extension and flexion perturbations had a displacement of 6°, a velocity of 60°/s, and a hold time of 250 ms after the end of the ramp. These characteristics resulted in a ramp duration of 100 ms, sufficient to elicit consistent long-latency stretch responses (Lewis et. al, 2005). To prevent fatigue a minimum of a 1-minute break was enforced between blocks.

Data Analysis

Muscle activity was quantified for the triceps and SCM muscles during all trials. The mean value was subtracted from the EMG collected in each trial. These were then rectified, and normalized by the maximum mean rectified EMG (0.5 s average) recorded during the MVCs performed at the start of each experiment. All data were aligned such that the onset of the perturbation (posture-maintenance phase), GO, and probe trials occurred at 0 s. All responses are reported as % MVCs, and changes in EMG amplitude are reported relative to the background activity prior to perturbation onset.

Three main time periods after each perturbation were evaluated: short-latency (25 – 50 ms), early long-latency (50 – 75 ms), and late long-latency (75 – 100 ms). These time bins were chosen to be consistent with our previous work (Lewis 2006, Krutky 2010), while also allowing the responses elicited in the long-latency time period to be assessed with greater

fidelity (e.g. Kurtzer 2008). The late long-latency window is also relevant for muscle activity elicited by startling acoustic stimuli, which have an onset within this range (Valls-Sole, 1999). The average amplitude during each of these time windows was calculated for each trial.

The onset of muscle activity was calculated for the triceps and SCM muscles in all trials. Onsets were detected as the time at which the evoked activity exceeded the background muscle activity by at least two standard deviations. These detections were first computed automatically, and then verified manually without knowledge of the corresponding trial type. For perturbation trials both short- and long-latency onsets were noted in the triceps. For MOV:EXT perturbations where the triceps muscle was shortened, the above method was used to find the onset of short-latency inhibition and the onset of long-latency excitation. For MOV:FLEX perturbations where short and long-latency responses were excitatory, the first point of inflection between the short-latency and the long-latency responses was used to quantify long-latency excitation.

All trials were evaluated for the presence of startle. SCM activity earlier than 120 ms following the auditory stimulus or perturbation onset was used as an indicator of startle, as employed previously (Carlsen et.al, 2010).

Statistical Analysis

Our primary hypothesis was that a perturbation of elbow posture, delivered after a ballistic movement has been prepared, can elicit startle and trigger the early release of the planned movement. We used activity in the SCM muscle as a marker of startle response initiation. We compared the probability of eliciting SCM activity when the participants had been instructed to prepare a movement (MOV conditions), and when they had not (DNI conditions). Two measures were used to evaluate if activity in the SCM was associated with the early release of the planned movement. First, we compared the onset latency of the activity in the triceps during voluntary movement to the long-latency activity evoked by each of our experimental probes (SAS, EXT, FLEX). Second, we assessed if the magnitude of this perturbation-evoked activity in the triceps was associated with the movement plan (MOV or DNI), or the characteristics of the perturbation (EXT or FLEX).

All statistical comparisons were made using linear mixed-effect models in which participants were treated as a random factor and all individual trials included in analysis. This method has been shown to be more rigorous and powerful than using a single mean for each subject (Montgomery, 2013). The use of all trials allows the variability contained within each experimental condition and each subject to be considered, and appropriately handles unbalanced data sets (Pinheiro and Bates, 2000). Analysis of variance was used to assess statistical significance of the factors within each model. Significance for all tests was evaluated against a p-value of 0.05. *Post hoc* comparisons were used to evaluate the difference between levels of all significant factors. Tukey's Honestly Significant Difference (TukeyHSD) was used to correct for multiple comparisons in these *post hoc* tests. All of the statistical analyses were performed using the *nlme* package in R (R Development Core Team, 2006).

We further hypothesized that the muscle response evoked by a perturbation delivered after the participant has prepared a movement can be explained as the sum of a stretch reflex generally opposing the applied perturbation and a startle-evoked response associated with the planned movement. This was assessed by comparing the EMG responses elicited in the presence of a movement plan (MOV:EXT and MOV:FLEX) to the algebraic sum of the stretch reflex elicited in the absence of a movement plan (DNI:EXT or DNI:FLEX) and the early release of a movement plan elicited by a startling acoustic stimulus (MOV:SAS). In

other words, the MOV:EXT condition was compared to the sum of DNI:EXT and MOV:SAS while the MOV:FLEX condition was compared to the sum of DNI:FLEX and MOV:SAS. The average amplitude was calculated for each condition and sum during the short-latency (25 – 50 ms), early long-latency (50 – 75 ms), and late long-latency (75 – 100 ms) time windows. A paired t-test was used to compare the average responses during each time window. Error bars in all figures represent standard deviations for the indicated group.

Results

Arm perturbations can evoke activity in the sternocleidomastoid muscle

Both startling acoustic stimuli and elbow perturbations consistently elicited activity in the SCM, an indicator of startle circuit activation, when delivered in the presence of a plan to extend the elbow ballistically. When a startling acoustic stimulus was delivered, it not only evoked activity in the SCM, but also led to an early initiation of activity in the triceps muscle and a corresponding early initiation of the planned elbow movement (Fig. 3A). Similar activity was evoked in the SCM when elbow perturbations were delivered in the presence of a movement plan (Fig. 3B,C). Neither startling acoustic stimuli nor elbow perturbations elicited activity in the SCM when participants were instructed not to respond to the perturbation (Fig. 3, gray traces).

As would be expected, the elbow perturbations also evoked stretch reflexes in the triceps. Flexion perturbations resulted in short- and long-latency excitation of the triceps; extension perturbations resulted in short-latency inhibition, both responses being consistent with a reflex response that resists the perturbation. In contrast, the long-latency component of the perturbation-evoked triceps response varied according to the instructions given to the participant rather than the characteristics of the perturbation. When the participant prepared an extension movement (MOV conditions), elbow perturbation produced an excitatory long-latency response in the triceps larger than that observed in the DNI conditions (Fig. 3B,C). This instruction-related increase in triceps activity occurred for both flexion and extension perturbations. When the perturbation was in the direction of the prepared movement (MOV:EXT condition), the long-latency activity in the triceps acted to assist rather than resist the perturbation.

The probability of eliciting activity in the SCM was compared across all five experimental conditions involving a probe stimulus (Fig. 4A). The probability differed significantly between these conditions ($F_{4,36} = 31.0$, $p < 0.001$), with all MOV being greater than DNI trials (all $p < 0.001$), demonstrating that SCM contraction was more likely to occur when a ballistic movement had been planned. On the contrary, the likelihood of SCM activation was not influenced by the type of stimulus used (SAS, FLEX or EXT: $p > 0.38$ for all MOV conditions, $p = 0.94$ for DNI conditions).

The average latency of the stimulus-evoked activity in the SCM was within the time range typically ascribed to the long-latency stretch reflex and faster when elicited through acoustic stimulus (Fig. 4B). The average latency varied significantly with the stimulus type ($F_{2,190} = 14.8$, $p < 0.0001$). The shortest latencies were observed in response to SAS (73.5 ± 25 ms), whereas longer SCM latencies were observed in response to the FLEX (87.5 ± 20 ms) and EXT (88.4 ± 19 ms) perturbations.

Instruction-dependent modulation of the stretch reflex

The instruction-dependent modulation of the stretch reflex occurred only within the late portion of the long-latency response (75–100 ms). This was observed for perturbations delivered in both directions (Fig. 5). The responses elicited in this time period were affected by both the direction of the perturbation (FLEX or EXT; $F_{1,445} = 97.61$, $p < 0.0001$) and the

instructions given to the participant (MOV or DNI; $F_{1,445} = 189.51$, $p < 0.0001$). The magnitude of the instruction effect (18.3% MVC) was approximately 50% greater than the magnitude of perturbation direction effect (12.9% MVC) within this time window. The interactions between these factors was smaller (6.1% MVC) and did not reach statistical significance ($F_{1,445} = 3.69$, $p = 0.06$).

The onset of the instruction-related triceps activity evoked by the three test probes was faster than that observed during voluntary movement (Fig. 6) but no difference was observed between MOV:SAS and MOV:EXT conditions. The onset of instruction-related triceps activity was different between each condition ($F_{3,1240} = 618.90$, $p < 0.0001$). There was no significant difference between the latencies observed in the MOV:SAS (73 ± 14 ms) and MOV:EXT (73 ± 12 ms) conditions ($p = 0.52$), but responses in these conditions were both slower than those observed in the MOV:FLEX (59 ± 8 ms) condition ($p = 0$). This is presumably because the FLEX perturbation elicited an excitatory long-latency stretch reflex that occurs earlier than the instruction-related response (Lewis et. al, 2005). In comparison to these early movement onsets, the average latency for triceps activity during voluntary movements was (173 ± 82 ms). Voluntary movements were significantly slower than all other conditions ($p = 0$).

Independence of plan- and perturbation-related responses

The EMG response to perturbations delivered after the participant had prepared a movement could be explained as a sum of a stretch reflex opposed to the joint perturbation and a startle-evoked response associated with the prepared movement (Figure 7). There was no significant difference between the amplitude of the triceps response recorded in the MOV:EXT conditions and a linear sum of responses in the MOV:SAS and DNI:EXT conditions (short latency: $\Delta = 0.03 \pm 0.81$, $p = 0.93$, early long latency: $\Delta = 0.05 \pm 1.68$, $p = 0.66$, late long latency: $\Delta = 3.24 \pm 6.42$, $p = 0.42$). Likewise, no significant difference existed between the triceps response in the MOV:FLEX condition and a linear sum of responses in the MOV:SAS and DNI:FLEX conditions (short latency: $\Delta = 0.27 \pm 0.20$, $p = 0.95$, early long latency: $\Delta = 1.44 \pm 1.89$, $p = 0.57$, late long latency: $\Delta = 0.99 \pm 7.51$, $p = 0.30$). These results are consistent with the existence of independent processes controlling the perturbation- and instruction-related responses to the applied perturbation.

Discussion

It has long been known that long-latency responses elicited by an external perturbation of posture can be modulated by how a subject is instructed to respond to the perturbation, yet the specific neural pathways responsible for this type of modulation remain unclear. The goal of this study was to determine if instruction-dependent reflex modulation is associated with activity in the brainstem pathways that contribute to the classic startle response. Specifically, we tested the hypothesis that perturbations of arm posture result in activation of the SCM, an indicator of startle circuit activation.

We found that postural perturbations could elicit activity in the SCM, but only when subjects had prepared a ballistic elbow extension movement. Postural perturbations and startling acoustic stimuli triggered activity in the SCM with the same probability. There was no significant SCM activity in response to either stimulus in the absence of a movement plan. When SCM activity was present, there was an associated early release of the planned movement, as evidenced by an onset of activity in the triceps muscle that was significantly earlier than that observed during volitional movements in response to non-startling stimuli. When SCM activity was present in response to a perturbation, there was a corresponding increase in muscle activation that was appropriate for the planned movement. This increase occurred in the late-long latency (75-100ms) time window, a period similar to the early

movement response triggered by acoustic startle (73.5ms). The direction of the perturbation-triggered response (excitatory or inhibitory) was independent of the direction of the perturbation (flexion or extension) indicating that it was not a feedback response appropriate for returning the limb to its original position. Finally, the EMG response to perturbations delivered after the participant had prepared a movement could be explained as a sum of a stretch reflex opposed to the joint perturbation and a startle-evoked response associated with the prepared movement. Prepared elbow extension movements were chosen to differentiate the results presented here from classic startle response, which typically results in elbow flexion (Honeycutt and Perreault, 2012; Valls-sole et al., 1997). However, these results are expected to extend to prepared elbow flexion movements which are also susceptible to early release via the startle reflex (Honeycutt and Perreault, 2012). Together, these results demonstrate that the rapid perturbations of posture can trigger the early release of a planned ballistic movement, and that this early release is associated with simultaneous activity in the brainstem pathways contributing to startle reflexes.

Early release of voluntary motor plan

Our results indicate that perturbations, applied after a voluntary movement has been planned, can elicit startle-like responses that result in the early release of the prepared movement. These findings support previous suggestions that long-latency stretch reflex modulation associated with how a subject is instructed to respond to a perturbation may be due to the early release of a prepared voluntary action. For example, Crago et al., (1976) came to this conclusion after observing activity in the biceps brachii as early as 70 ms after the onset of shortening of the same muscle. Rothwell et al., (1980) also suggested that long-latency stretch response modulation observed during action preparation in the biceps was due to interaction between the long loop stretch reflex response and a subsequent “rapid voluntary event”, since reflex modulation was reduced when the timing of the perturbation was unpredictable. More recently, it has been demonstrated in both single-joint and multi-joint studies in the human upper limb that the long-latency stretch reflex exhibits characteristics of an impending voluntary movement (Koshland and Hasan, 2000; Pruszynski et al., 2008; Pruszynski et al., 2011b). None of these studies, however, has assessed the neural pathways involved in the superposition of reflex and voluntary responses to limb perturbations.

Our observation that long-latency stretch reflex modulation during movement preparation is accompanied by activation of the SCM muscle suggests that the neural circuits responsible for auditory startle responses are also involved in releasing prepared voluntary actions in response to a perturbation. We found that the response of the triceps brachii to elbow perturbations could be estimated as a linear sum of the stretch reflex response when the participant was instructed to “not to intervene” and the response to a startling acoustic stimulus prior to the onset of a planned movement. This linear summation strengthens our conclusion that the earliest muscular responses to postural perturbations often incorporate contributions from both a perturbation-dependent reflex and an instruction-dependent startle-like response. Similar conclusions regarding the heterogeneity of pathways contributing to long-latency stretch reflexes, and the superposition of their outputs, were reported by Pruszynski (Pruszynski et al., 2011b), using an experimental task similar to our own. Here, we extend those results to consider the pathways involved in the early release of the planned movement.

It has been previously suggested that the modulation of the long-latency stretch reflex in response to subject instructions resulted from a feedback mechanism related to perturbation characteristics (Pruszynski et al., 2011b). That conclusion was based on the finding that the average response associated with the planned movement scaled with the magnitude of the perturbation. However, planned movements triggered by acoustic stimuli are also known to

scale with perturbation magnitude, and there are two independent components to this phenomenon: an influence of stimulus intensity and an influence of startle (Carlsen et al., 2007). At matched intensities, the acoustically triggered movements are faster and larger when accompanied by indicators of startle. The probability of eliciting a startle increases with perturbation intensity. Hence, the change in the average perturbation response reported by Pruszynski et al. (2011b) may simply reflect the change in the probability of eliciting a rapid release of the planned movement when using perturbations of different amplitude, or that combined with an intensity effect. Our data clearly show that when a planned movement is triggered early, it is independent of the direction of the applied perturbation – always in the direction of the movement plan rather than opposed to the perturbation – a result consistent with other studies (Crago et al, 1976; Gottlieb and Agarwal, 1980). We also demonstrated that a startling acoustic stimulus delivered in the absence of a perturbation triggers an early release of the planned movement very similar to that triggered by a perturbation. Together, these results argue strongly against a long-latency reflex that is only a feedback response to the perturbation.

This is not to suggest that there are not perturbation-related feedback components to long-latency stretch reflexes, as they have been demonstrated in many studies, including our own (Kimura et al., 2006; Krutzer et al., 2008; Shemmell et al, 2009; Pruszynski et al., 2011a). It is important to note that the data presented here represent responses to perturbations that activate startle circuits a majority of the time. For perturbations or other experimental conditions that do not activate these circuits, it is likely that perturbation-related feedback pathways would dominate the elicited response. The present findings highlight the need to consider the multiple pathways that can contribute to reflex responses in the long-latency time period, and emphasize the importance of interpreting these reflexes and their associated pathways in a task-specific manner. Investigating the conditions that most reliably activate each mechanism would be an important extension of the present work.

Contributions from subcortical pathways to perturbation response

It is likely that all layers of the nervous system contribute to the dynamic response resisting a perturbation. For example, Evarts and Tanji (1976) observed instruction-dependent modulation of perturbation responses in pyramidal tract neurons recorded from non-human primates performing tasks very similar to the MOV task in the present study indicating that the cortex is a likely contributor during these responses. In addition, when the cortex is damaged following a stroke, load-dependent feedback, which has been associated with motor cortical involvement, is impaired (Trumbower et. al, 2013). Still, the similarity between triceps responses evoked by elbow perturbations and those evoked by startling acoustic stimuli suggests that the perturbation-evoked early release of a planned motor action is mediated at least in part by startle circuits in the brainstem.

Davis et al. (1982) proposed a five-synaptic acoustic startle pathway in rats involving the reticular formation (specifically, the nucleus reticularis pontis caudalis) of the brainstem. Lingenhöhl and Friauf, (1994) reduced this further to a three synaptic pathway, with direction connections between the cochlear nucleus and the reticular formation. In addition to receiving acoustic inputs, the reticular formation is also known to receive vestibular and tactile (especially from the trigeminal nerve) inputs (for review, see Yeomans et al., (2002)). These additional sensory inputs to the reticular formation can trigger startle-like responses in animals. Stapley and Drew (2009) showed activity in feline reticular formation immediately preceding a startle-like response triggered by removal of the support surface during standing. In non-human primates, neurons in the reticular formation show activity that corresponds to both preparatory and movement related activity during reaching tasks (Buford and Davidson, 2004). Together with our results, the literature suggests that an early

release of a planned movement can be triggered by a startling perturbation, in a manner similar to the triggering that has been reported when using a startling acoustic stimulus.

The role of the brainstem in the early release of planned movement in response to a startling stimulus has been primarily investigated in animal models; however there is growing evidence that similar circuits are involved in humans. Startling acoustic stimuli can still be used to elicit the rapid release of prepared movements in individuals with cortical lesions resulting from stroke (Honeycutt and Perreault, 2012). Further, instruction-dependent modulation of the long-latency reflex in unimpaired subjects, as observed in the present study, is not impacted by TMS suppression of the primary motor cortex (Shemmell et al., 2009). These studies suggest the importance of subcortical structures when responding to startling stimuli.

Interestingly, SCM activation indicating a startle had occurred was delayed during MOV:EXT and MOV:FLEX in comparison to MOV:SAS trials. While it is reasonable to expect that the delay in SCM activity would result in a corresponding delay in peripheral muscle activation, previous work has not been able to demonstrate a correlation between SCM and agonist muscle latencies during acoustic-triggered startle movements (Carlsen et al., 2004a,b). Animal studies also demonstrate that activity recorded from the reticular formation during postural perturbation is relatively invariable in latency while muscle activation in the periphery has 3-4 times as much variance (Stapley and Drew, 2009). Our findings are the same. Despite different SCM latencies, there was no difference between the agonist latencies in the MOV:SAS and MOV:EXT conditions (Figure 6). The lack of a relationship suggests that any brainstem circuits that might be involved in the activation of SCM and the rapid release of a planned motor action are not activated simultaneously. It also highlights the need to obtain more direct measures of brainstem activity for elucidating its potential role in the rapid release of planned motor actions.

Functional Implications

The results of this study demonstrate that limb perturbations applied after a movement has been planned consist of a posture-stabilizing reflex response opposed to the perturbation, and a perturbation-evoked release of the prepared movement. Specifically, our data suggest that in addition to trans-cortical stretch reflex pathways that have been shown to mediate feedback responses (Kimura et al., 2006; Shemmell et al., 2009; Pruszynski et al., 2011a), subcortical circuits mediating the acoustic startle response can also contribute to the long-latency response to limb perturbations. The relative contributions from these pathways almost certainly vary in according to the requirements of the task being performed. Finally, these results indicate that similar mechanisms may prove valuable during larger, balance-challenging perturbations of the whole body, where the brainstem (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) has acknowledged importance and startle triggered movement have just begun to be evaluated (Blouin et al., 2006; Campbell et al., 2012; Seigmund et al., 2008).

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Figure 1.

Setup used for the experiment. The shoulder straps and the lap belt used for restraining the participant are not shown in the figure. The shoulder horizontal flexion was at 0° and the wrist was slightly pronated. The rest of the joint angles are shown in the figure. The audio speaker was used to deliver the WARNING and GO tones, while the loud speaker was used to deliver the Startling Acoustic Stimulus. Position perturbations were applied by the motor.

Figure 2.

The schematic of the timeline of the experiment. The different types of trials used in the experiment are depicted. During the posture maintenance phase, participants received 20 flexion (FLEX) or extension (EXT) perturbation, in a randomized order. During the 180 voluntary movement trials, participants got into the Home position, waited for the WARNING signal, then prepared to move to the Target position as soon as they received the GO signal. In 10 SAS trials, participants received a startling acoustic stimulus, coincident with the GO. In perturbation trials, participants given a flexion or extension perturbation (10 trials each) coincident with GO.

Figure 3.

Average joint angle (top) and EMG response from the triceps (middle) and SCM (bottom) muscles. A) Data from MOV:SAS (black) probe trials are graphed with MOV:VOL (gray). B) Data from MOV:FLEX (black) and DNI:FLEX (gray). C) Data from MOV:EXT (black) and DNI:EXT (gray).

Figure 4. SCM activity across conditions. A) Probability of SCM activity prior to 120ms during probe and DNI trials. B) SCM muscle onset latency during probe trials.

Figure 5.

Average Triceps activity during DNI (black) and MOV (gray) trials during short latency (25 - 50ms), early long latency (50 - 75ms) and late long latency (75 - 100ms). A) Extension perturbation. B) Flexion perturbation

Figure 6.

Average onset of triceps activity during MOV:SAS and MOV:VOL compared to the onset of the long latency triceps latency during MOV:EXT and MOV:FLEX trials

Figure 7.

A) Average triceps activity during MOV:SAS (black) and DNI:FLEX (light gray). B) Average triceps activity during MOV:SAS (black) and DNI:EXT (light gray). C) Comparison of probe trial MOV:FLEX (dark gray) to the sum of DNI:FLEX and MOV:SAS (dashed black). D) Comparison of probe trial MOV:EXT (dark gray) to the sum of DNI:EXT and MOV:SAS (dashed black).