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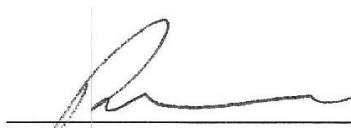
October 24th, 2019

Dear Dr. Steindel,

Please consider our manuscript titled '***A modified lean and release technique to emphasize response inhibition and action selection in reactive balance***' for publication as a research article in the ***Journal of Visualized Experiments***. This is a revision to address comments and questions expressed by three expert reviewers and the editorial team.

In this submission we offer a novel approach to change features of the response environment to emphasize higher brain processes in the control of reactive balance. Specifically, this method demands rapid inhibition of an automatic postural response while simultaneously forcing the participant to choose a more suitable corrective action to avoid a forward fall (e.g. reaching to grasp a secure handrail instead of stepping forward into a block). Insight gained from this technique could shed light on cognitive deficits contributing to falls and could potentially be applied as a training tool to improve behavioral flexibility as it pertains to maintaining balance in a complex, choice-demanding environment.

Sincerely,



Signature

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TITLE:

A Modified Lean and Release Technique to Emphasize Response Inhibition and Action Selection in Reactive Balance

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KEYWORDS:

balance, posture, lean & release, cognition, response inhibition, decision-making, falls

SUMMARY:

Here we offer a protocol that allows the user to selectively change affordances and/or constraints on movements that are relevant for recovering balance after postural perturbation.

ABSTRACT:

Assessment of reactive balance traditionally imposes some type of perturbation to upright stance or gait followed by measurement of the resultant corrective behavior. These measures include muscle responses, limb movements, ground reaction forces, and even direct neurophysiological measures such as electroencephalography. Using this approach, researchers and clinicians can infer some basic principles regarding how the nervous system controls balance to avoid a fall. One limitation with the way in which these assessments are currently used is that they heavily emphasize reflexive actions without any need to revise automatic postural reactions. Such an exclusive focus on these highly stereotypical reactions would fail to adequately address how we can modify these reactions should the need arise (e.g., avoiding an obstacle with a recovery step). This would appear to be a glaring omission when one considers the enormous complexity of the environments we face daily. Overall, the status quo when evaluating the neural control of balance fails to truly expose how higher brain resources contribute to preventing falls in complex settings. The present protocol offers a way to require suppression of automatic, but inappropriate corrective balance reactions, and force a selection among alternative action choices to successfully recover balance following postural perturbation.

INTRODUCTION:

Despite the recognized correlation between falls and cognitive decline¹⁻³, a major gap persists in understanding what the brain actually does to help us avoid a fall. In theory, cognitive demands would be accentuated as environmental complexity increases and in situations where we need

to revise instinctive behavior. However, most balance tests fail to effectively tax higher brain function, instead emphasizing reflexive righting reactions. While factors such as response speed are essential to prevent a fall, additional cognitive factors, such as inhibitory control and/or the ability to select appropriate action based on a given context may also be important in certain situations. As a result, one reason we may fail to understand the brain's role in reactive balance is due to research protocols currently in use. Rogers et al. recently summarized the different ways in which balance control has been assessed using external perturbation⁴. These methods include platform translation, tilts and/or drops, as well as the use of automated systems that push, pull, or remove postural support. Despite the large variety of techniques used to disrupt upright equilibrium, the ensuing corrective reactions are almost always made in an unobstructed environment, thus minimizing constraints on movement. Here, we propose a method where cognitive processes are required to override prepotent action and select suitable responses among alternatives in a reactive balance task.

A common way to test reactive balance is to impose relatively small postural perturbations that can be countered using a fixed support (typically feet-in-place) reaction⁵⁻⁹. Comparatively fewer studies have focused on change-of-support balance reactions in response to perturbations via waist pulls, platform translation, and release from a support cable. As an example, see Mansfield et al.¹⁰. The importance of the latter group can be appreciated by recognizing that when perturbations are large, change-of-support reactions are the only option to recover stability¹¹. In fact, even for smaller perturbations that could be managed using feet-in-place (i.e., hip and/or ankle) strategies, people frequently prefer to step when given the choice¹¹. The value in studying such change-of-support reactions lies not only in the fact that a greater magnitude of perturbation must be countered, but also the challenges that emerge when repositioning the limbs to establish a new support base. The presence of affordances and/or constraints on action are a regular part of many real-world settings. This forces a selection process to establish a new base of support when a loss of balance occurs. To adapt behavior to complex environments, there is a heightened demand on higher brain resources. This is especially true when the limbs must establish a new base of support. To emphasize and expose cognitive roles in reactive balance the need to reintroduce clutter and force a change-of-support strategy with the limbs seems logical.

One simple way to deliver an externally induced postural perturbation is the lean & release technique, where an individual is suddenly released from a supported forward lean. This approach allows assessment of compensatory reactions to avoid a forward fall and has been successfully used in both healthy and clinical populations¹²⁻¹⁴. Although the lean & release technique is somewhat basic, it offers valuable insight into reactive balance capacity (e.g., how quickly someone can initiate a recovery step, or to determine the number of steps required to regain stability). For present purposes, the lean & release technique provides a simple way to explore cognitive roles in reactive balance because many of the perturbation characteristics are held constant. This provides greater experimental control over variables specifically relevant to action selection and response inhibition. While other modes of postural perturbation typically rely on unpredictability in terms of perturbation direction, amplitude, and timing, the surrounding environment is always constant. Even in studies where leg blocks have been used to emphasize reach-to-grasp reactions¹⁵ the blocks are fixed in place with no need to quickly adapt

stepping behaviors based on the presence or absence of a leg block. With the presently proposed method, we can change the environment in a way that demands behavioral adaptation to avoid a fall.

Beyond laboratory settings that inadequately expose cognitive roles in reactive balance, another major issue is a heavy reliance on external measures such as muscle onsets, ground reaction forces, and video motion capture to infer neural processes. While these measures are valuable, exclusive reliance on such measures fails to provide direct insight into the underlying neural mechanisms that contribute to balance. This problem is compounded when considering that much of what the brain may do to prevent a fall in complex environments likely happens before the fall. Predictive roles in fall prevention have recently been discussed more extensively¹⁶. Research directions include predicting future instability¹⁷, building visuospatial maps as we move through our environment¹⁸, and possibly forming contingencies based upon the environment even without foreknowledge of a fall¹⁹. Revealing such preparation would be entirely inaccessible without use of direct neurophysiological probes.

The modified lean & release approach as presently proposed offers a means to overcome some of the existing limitations mentioned. This is done by using a testing scenario where the limbs are required to establish a new base of support in a choice-demanding environment. This approach is augmented by including direct measures of brain activity (e.g., transcranial magnetic stimulation, TMS) both before and after postural perturbation, which can complement external measures of force production and motion capture. This combination of experimental features represents an important innovation in the field to expose how the brain contributes to balance in complex settings where response inhibition and selecting actions among options are called for to prevent a fall. Here we demonstrate a novel method for testing reactive balance in a setting that emphasizes the need for cognitive processes to adapt behavior in order to avoid a fall. The combination of obstacles and affordances for action force the need for response inhibition, targeted action, and response selection among options. Moreover, we demonstrate precise temporal control over visual access, timing of neural probes, changing the response environment, and onset of the postural perturbation.

PROTOCOL:

All procedures received approval from the Institutional Review Board at Utah State University and were conducted in accordance with the Declaration of Helsinki.

1. Participant screening

1.1. Have participants provide written informed consent to procedures prior to testing.

1.2. For testing with TMS, screen participants prior to testing in order to assess their suitability for TMS using guidelines developed by a group of experts²⁰.

2. Data acquisition: electromyography (EMG)

2.1. Record EMG using surface electrodes and amplify signals (gain = 1,000; see **Table of Materials**).

2.2. Acquire data and bandpass filter (10–1,000 Hz) using a data acquisition interface and appropriate software (see **Table of Materials**). Use this device and software to control the various motors, cable release, and occlusion goggles as described later in the methods.

2.3. Gently abrade the skin surface and wipe with alcohol over the target muscle locations. Fix the surface EMG electrodes onto the target muscles using two-sided tape, and further secure using prewrap to ensure that the electrodes remain fixed, especially during rapid responses with the arms and legs.

2.4. Collect EMG data from two intrinsic hand muscles on the right hand (first dorsal interosseus, FDI and opponens pollicis, OP) and ankle dorsiflexors on both legs (tibialis anterior, TA).

NOTE: These particular muscles were selected based on their relevance to a reach-to-grasp action or a forward step, but other muscles could be selected as needed.

3. Balance testing equipment

3.1. Modified lean & release system

3.1.1. Use a custom-made, lean & release cable system to impose forward perturbations (see **Figure 1** and **Figure 2**).

[Place Figure 1 here]

[Place Figure 2 here]

3.1.2. Have participants stand in a forward lean position with their feet approximately hip width apart (see **Figure 3**). Maintain this forward lean using a body harness attached to a cable, which is then secured to the wall behind them. Fasten the cable to the back of the harness (approximately midthoracic level). Fix the support cable to the wall by a magnet. The magnet will be briefly deactivated to release the cable.

3.1.3. Make the specific trial procedures (i.e., when the cable is released and the onset of the cable release) unpredictable to the participant. Control the precise timing of cable release via computer commands preset into a software configuration. This configuration will allow control of the timing of cable release so that it can be randomized across trials.

NOTE: The software configuration that controls all experimental devices (e.g., triggering the motor to position a leg block) sets the specific trial condition (e.g., if a leg block is present or not).

This can be programmed to randomize conditions or deliver them in blocks to control the level of predictability.

3.1.4. In addition to this release cable attached to the back of the harness, also secure participants to a support cable hanging from the ceiling. This failsafe cable provides no bodyweight support unless absolutely necessary. If a participant is unable to recover balance on their own, the cable catches them before falling to the ground.

3.1.5. Due to the importance of reliable visual information, verify that participants can actually see the handle and leg block when wearing the goggles. Begin each trial by instructing participants to look directly at a fixed point on the floor, about 3 m in front of them, while holding their head in a comfortable position. Position the participants such that their gaze is set to view the handle in the peripheral visual field and the top portion of the obstacle.

3.1.6. Position the body to ensure that the handle is within graspable range. Have the participant lean forward while keeping both feet in contact with the floor. This will require rotation about the ankle while the rest of the body remains in a straight line.

3.1.7. Determine the specific lean position as the minimal lean angle where a forward step is necessary to recover balance when the cable is released. This is an iterative process to find a threshold lean angle at the ankle joint, which is the angle where the participant is no longer able to prevent a forward fall using a feet-in-place reaction. Once this is established, verify the lean angle throughout testing using goniometry.

3.2. Affordances and constraints on compensatory balance responses

3.2.1. Fix a safety handle onto the wall beside participants on their right side. Use a motorized cover to control access to this handle. If the handle is uncovered, when the participants are released from their supported forward lean it can be used to regain balance.

3.2.2. During trials where the handle is uncovered, place a leg block in front of the participant's legs. The leg block impedes a step, but is not rigidly set in place, meaning that it can be displaced when kicked. Program the leg block to allow free movement and construct it with compliant material to avoid injury.

NOTE: The leg blocks have been constructed to force an 'all-or-none' step decision given that they rise almost 30 inches off the ground (mid-thigh level on most individuals). For researchers interested in a more nuanced blockade of a recovery step, these devices could be modified to use a smaller/shorter obstacle that would then allow an adapted step to clear them.

3.2.3. Use a black tarp to cover the handle and block it from view on certain trials. The handle will remain mounted at the same location but will be physically covered to prevent direct visual access and to prevent any supportive grasp. When this support handle is covered, remove the leg block to allow a step reaction if necessary.

3.3. Control of vision

3.3.1. Limit vision to the time frame just before postural perturbation and control via liquid crystal goggles (see **Table of Materials**). When closed, the goggles prevent access to the visual scene so participants are unaware of the forthcoming response condition.

3.3.2. Change the specific configuration of the leg block and handle availability for each trial while the goggles are closed so that participants need to quickly perceive the environment once the goggles open. Move the handle cover and the leg block into position via computer-triggered, servo motors at the start of each trial. Have the participants wear ear plugs and make motors move continuously during the period of visual occlusion to avoid any advanced cueing for the upcoming condition.

4. Experimental design

4.1. Prior to testing, briefly familiarize participants with how to reach the handle and step forward from a leaning position.

4.1.1. Provide participants with full knowledge of the upcoming practice condition and make sure there is no uncertainty. Instruct the participants that once the goggles are open, they will see the handle covered, and the stepping path will be clear. Shortly after, the support cable will release and they will have to step quickly to avoid falling forward.

4.1.2. Use similar instructions regarding whether or not the handle is available for grasping to avoiding a step.

4.1.3. Throughout testing and practice, instruct the participants to remain relaxed unless prompted to move by a sudden cable release.

NOTE: On average, participants require approximately 10 practice attempts before formal testing begins.

4.2. Randomly change the response setting between trials. If released from the support cable, participants must regain stability by either reaching for the wall-mounted safety handle or stepping forward if the step path is clear.

4.3. Always close the occlusion goggles at the beginning of each trial, at which time the response setting will be altered. Close the goggles for a randomized period (usually about 3–4 s) to allow the setting to change.

4.4. When the goggles open, provide one of two possible response settings: (1) the leg block is present and the support handle is present, or (2) no leg block is present and no support handle is present.

NOTE: In the first condition, a support handle is available at a comfortable reach distance and the leg block prevents a step. This setting imposes a context where the only option available is to quickly grasp the available support handle with their right arm. The second condition allows for a recovery step while preventing use of the support handle.

4.5. On trials where a perturbation does occur, release the cable shortly after the goggles open. This delay period will vary with study requirements, but ranges from 200–1,000 ms.

4.6. For some trials, do not release to act as a catch trial. This helps avoid anticipatory responses based only on vision.

4.7. Have each trial last 10 s, with a short pause between trials to allow participants a chance to reset as needed. Give participants a brief rest period in between each test block and allow them to sit. The basic experimental design is depicted in **Figure 3** (bottom).

[Place Figure 3 here]

NOTE: The total trial number is varied to suit the needs of each study but tends to include approximately 100 trials divided across three to four test blocks.

5. TMS protocol (optional)

5.1. Deliver single-pulse TMS over the hand motor cortical representation while participants are supported in a forward lean. Deliver TMS pulses shortly after opening the goggles but prior to any movement to investigate how viewing the environment impacts the motor set. See **Figure 3** to visualize the sequence of events during a trial, including when TMS is delivered.

5.2. Set the timing for TMS delivery according to the research question. In the representative results, stimulation varied between 100 ms and 200 ms post-vision. In addition to the response settings listed above, randomly intersperse ‘no-vision’ reference trials throughout testing to deliver TMS without opening the goggles. The purpose of this condition is to provide a baseline for any task-related changes in motor activity (e.g., increased arousal).

NOTE: Further details on the specific TMS procedures can be found in Bolton et al.²¹ and Goode et al.²².

5.3. Deliver magnetic stimuli to the primary motor cortex (M1) with the stimulating coil oriented approximately 45° to the sagittal plane (see **Table of Materials**). Apply stimuli at the optimal position to obtain a motor evoked potential (MEP) in the FDI muscle on the right hand (i.e., the motor ‘hotspot’).

5.4. Once the ‘hotspot’ is found, determine a test stimulus intensity is determined. For the current research purposes, this is the stimulus intensity where the average MEP is approximately

1–1.5 mV peak-to-peak. Fix the TMS coil on this location and reset the coil position if head motion occurs (e.g., following cable release). Determine the test stimulus intensity while subjects stand in forward lean to account for any postural state influence on corticospinal excitability.

REPRESENTATIVE RESULTS:

All exemplar studies presented were conducted with young women and men between 18–30 years of age. The total sample size for each study was as follows: Example 1 (Rydalch et al.²³) included 12 participants, Example 2 (Bolton et al.²¹) included 63 participants, and Example 3 (Goode et al.²²) included 19 participants. The reader should refer to the complete studies for details on methods and analyses.

Example 1

Blocking a rapid recovery step, particularly when stepping was made automatic by frequent repetition, allowed for assessment of response inhibition in a postural context. Here, we compared the leg muscle response when a forward step was either allowed or obstructed²³. The muscle response from the stepping leg was compared between trials where the participant *should reach* versus trials where they *should step*. This was accomplished by comparing the response magnitude of ankle dorsiflexors (tibialis anterior) during reach-to-handle versus step trials. Specifically, the integrated EMG over a 200 ms window (i.e., 100 ms to 300 ms post-perturbation) was used to calculate a muscle response ratio. A smaller value indicated a greater ability to refrain from stepping as described in detail in Rydalch et al.²³. By using the magnitude of the muscle response, our intention was to provide a sensitive gauge for a tendency to respond with the leg. In this example, the goal of our study was to determine if response inhibition measured with a seated cognitive test (i.e., stop signal task, SST) correlated with performance on a reactive balance task where suppression of a balance recovery step was required. In the balance task, a total of 256 trials were collected, of which 30% used a leg block. In **Figure 4A**, we highlight averaged waveforms of individuals that were on opposite ends of the continuum for suppressing step-related leg activity. The scatterplot in **Figure 4B** depicts a small, but significant correlation between the ability to suppress a blocked step and response inhibition as measured by the stop-signal reaction time.

When interpreting these results, it is important to recognize that the SST (described in the Appendix), and indeed most cognitive tests, rely on simplistic responses (often finger movements) made by seated participants in response to imperative cues displayed on a computer screen. This study by Rydalch et al. addressed if the ability to stop a prepotent response was preserved across a standard seated test of response inhibition compared with a reactive balance test where compensatory steps must be occasionally suppressed²³. The results showed a correlation between the cognitive test outcome (stop signal reaction time) and compensatory stepping, which suggests that an individual's stopping capacity generalizes across diverse tasks.

[Place Figure 4 here]

Example 2

This study exemplifies how our modified lean & release setup when combined with TMS can be

used to study motor preparation based on vision. The concept of affordances (originally proposed by Gibson²⁴) was tested in a standing postural context, to determine if corticospinal excitability of a hand muscle (used for grasping) was facilitated when viewing a supportive handle. The key to this approach was assessing how the excitatory state of the motor system was affected by vision alone. Specifically, TMS pulses were delivered shortly after the goggles opened, but prior to any cue for movement (i.e., cable release). In this manner only the motor activity related to the visual scene was analyzed while the behavioral response to perturbation was secondary. Unlike the above study, which emphasized the need for response inhibition by presenting the step response more frequently, this study used an equal probability of handle (reach) vs. no-handle (step) to focus on visual priming of hand action. Results indicated that viewing the handle resulted in facilitation of an intrinsic hand (i.e., grasping) muscle but only in the pure observation condition (**Figure 5**)²¹. NOTE: For exemplar data, acquisition, and analysis software code, along with guidance notes please refer to the open science framework (<https://osf.io/9z3nw/>). Examples 1 and 3 used similar code and procedures, with modifications to specific states.

[Place Figure 5 here]

Example 3

This final example emphasizes how we adapted this device to once again study motor preparation of a hand muscle based on vision but focused on the need to quickly suppress leg action. In this version, the handle cover was permanently covered, while only the leg block moved. Like example 1, the probability of stop versus step conditions was manipulated to encourage an automatic step. Given that the handle was no longer an option in this study, the degree of forward lean measured at the ankle was slightly reduced (~ 6° vs. ~10° as in the above two studies) to allow a fixed support reaction. The specific use for this version of the task was to investigate the concept of global suppression, which has previously been explored in seated tasks where focal button presses were used in response to visual stimuli presented on a computer display²⁵. Like example 2, TMS was delivered to assess corticospinal excitability in an intrinsic hand muscle immediately following access to the response environment (i.e., block or no block), but prior to any cue to move (i.e., cable release). The rationale for testing an intrinsic hand muscle in a task that only used leg responses was to see if a task irrelevant muscle would show evidence of a general suppression throughout the motor system. The results depicted below in **Figure 6** show evidence of a widespread shutdown across the motor system when an automatic step is abruptly stopped²².

[Place Figure 6 here]

FIGURE AND TABLE LEGENDS:

Figure 1. Lean & release setup with leg blocks. In this example, one leg block is set in the open position, while the other is set to prevent a step. These blocks are moved via computer-controlled motors (grey boxes attached to the support posts). Handle covers are also moved to either block or allow a reach-to-grasp response. Here, the covers are detached to allow full view of the handle. The release magnet is visible on the back wall. All the wiring feeds through the wooden platform itself and enters into the grey circuit box located on the back corner.

Figure 2. Lean & release setup with force plates. This figure depicts how three force plates can be optionally embedded into the wooden platform. If force plates are not required, wooden plugs can be set in place. These plugs are visible, leaning on the side wall. This image also shows the safety harness worn by participants. This harness is secured to the ceiling to act as a safety mechanism should the participant fail to recover their balance on their own.

Figure 3. TMS-based method to investigate the impact of perceiving environmental affordances and/or constraints on motor preparation. TOP. A lean & release apparatus released participants in an unpredictable manner (perturbation test blocks only). The magnitude of perturbation required a rapid change-of-support reaction, using either the arm or leg to re-establish a stable base of support by either reaching to a secure handhold, or taking a forward step. In between trials, vision was occluded using liquid crystal occlusion spectacles and objects in the foreground were rearranged at random. **BOTTOM.** The timeline depicts when visual access to the environment became available and the timing of TMS probes relative to both visual access and the perturbation. The peak-to-peak amplitude of the muscle response to TMS (i.e., motor evoked potential, MEP) provided an index of corticospinal excitability in the time period before perturbation. This figure presents theoretical response data to demonstrate the hypothesized impact of an affordance for hand action (solid, blue line) versus a trial where the handle is covered (dotted, red line). In this figure, both trials/conditions are overlaid to illustrate the hypothesized effect of preparing motor output to either facilitate or suppress potential action based on a particular environmental context. Adapted from Figure 1 in Bolton et al.²¹. Note that TMS was used to probe corticospinal excitability in this example. However, this is only intended to provide a basic representation of the sequence of events using this modified lean & release.

Figure 4. Average step leg response. (A) Average waveforms are shown for the tibialis anterior in the stepping leg. Step trials are shown in red and reach trials in black. Exemplar muscle response data shown for two participants with either a fast (top) or slow stop (bottom) signal reaction time. This stop signal reaction time offers a millisecond measure of stopping ability. The early muscle response (integrated EMG) was measured from 100–300 ms (light yellow shaded region). **(B)** Scatterplot showing the correlation between the muscle response ratio and stop-signal reaction-time (SSRT) at the 400 ms visual delay, $r = 0.561$; $p = 0.029$. Adapted from Figures 3 and 5, Rydalch et al.²³.

Figure 5. Data showing the difference in corticospinal excitability for the REACH (i.e., handle) versus STEP (i.e., no-handle) trials in an intrinsic hand muscle while participants stood in a supported lean. This showed greater activity in the hand when the handle was present and participants simply viewed the handle (OBS) but this effect was absent during a separate balance (BAL) trials blocks where the cable was periodically released. Error bars show the standard error of the mean. Two-way repeated measures ANOVA revealed an interaction between condition and affordance, $F_{1,62} = 5.69$, $^{\#}p = 0.020$. To address our specific hypotheses, we used prior planned comparisons to determine if MEP amplitude in the FDI was greater when the handle was present within each condition separately. For hypothesis 1, planned comparisons were used to compare levels of affordance (STEP, REACH) within the OBS condition and revealed a significant increase

in amplitude when the handle was visible, $t_{121} = 2.62$, $*p = 0.010$. For hypothesis 2, we had originally predicted an interaction, but in the opposite direction from what was found. Planned comparison of affordance within the BAL condition showed no significant difference related to the presence of a handle, $t_{121} = -0.46$, $p = 0.644$. Adapted from Figure 5, Bolton et al.²¹.

Figure 6. Modified lean & release task with leg block only (i.e., no option for grasping a support handle). (A) This figure depicts MEP amplitude suppression in an intrinsic hand muscle when a leg block was presented (i.e., NO-STEP condition). (B) From the repeated measures ANOVA, the step condition x latency interaction, $F_{1,18} = 4.47$, $p = 0.049$, was significant. Visual inspection of the line graph 2 reveals decreasing MEP amplitude over time for the NO-STEP condition only and this was confirmed with follow-up comparisons. Specifically, these comparisons revealed a significant decrease at 200 ms compared with 100 ms $t_{18}=2.595$, $*p = 0.009$ for the NO-STEP condition. By contrast, a similar comparison between 200 ms and 100 ms for the STEP condition reveals no difference $t_{18} = 0.346$, $p = 0.367$. Adapted from Figures 1 and 2, Goode et al.²².

DISCUSSION:

This modified lean & release system provides a novel way to assess cognitive roles in reactive balance. As with the standard lean & release procedure, the direction and amplitude of postural perturbation are predictable to the subject while the timing of cable release is unpredictable. What is unique in the current approach is that access to vision is precisely controlled while the subject remains fixed and the response environment is altered around them to create different action opportunities and/or constraints. By manipulating the presence of obstacles and affordances this method emphasizes cognitive processes such as decision-making (i.e., action selection) and response inhibition in relation to balance recovery.

The proposed method has potential to provide a unique glimpse into the neural control of balance but poses certain limitations. For example, when using the lean & release method, the cable release is initiated from a forward lean, which necessitates a pronounced balance recovery step compared with other methods of external postural perturbation¹⁰. Also, the direction and magnitude of the perturbation are predictable, which may lead to anticipatory activation of muscles that would normally not be engaged in more realistic fall scenarios. Finally, vision is temporarily occluded prior to cable release, which also deviates from an individual's day-to-day experience. These features make our assessment of balance somewhat artificial and may preclude generalization across different modes of perturbation. It is important to recognize that generalizability to real world falls is always a concern when drawing inferences on how balance is controlled from any one particular assessment method. Indeed, a commonly recognized comprehensive test for balance ability does not currently exist⁴. For present purposes, a set forward fall allows perturbation characteristics and response settings to be held constant while manipulating specific cognitive demands that are often neglected or inaccessible in traditional balance assessments. Such experimental control is beneficial but should be taken into consideration when interpreting results.

As a second limitation, the construction of the testing equipment and the requisite engineering skills may represent a challenge to implement this method. Three electrical engineering students

from Utah State University built the platform, set up the electronics, and programmed microcontrollers to drive servo-motors for the handle cover and leg block. Construction costs were modest (i.e., <\$15,000 not including the force plates mounted into the platform). Nevertheless, this may pose a challenge depending on available resources.

Specific insights into the neural control of balance were obtained using this approach. These examples indicate that noninvasive brain stimulation can be used to capture motor set based on viewing objects in a postural context and offer a technique to assess response inhibition using muscle responses. Notably, the modified lean & release technique could be easily adapted to incorporate other neurophysiological probes such as electroencephalography and functional near-infrared spectroscopy. Even without the inclusion of direct neural measures, study designs that focus entirely on external forces, muscle activation, and kinematics can provide important insight into behavioral markers of cognitive deficits. For example, an interesting application for using force plates to capture anticipatory postural shifts during a reactive stepping task has been demonstrated by Cohen et al.²⁶. In their study, deficits in response inhibition in older adults were revealed by inappropriate weight shifting, which in turn led to delays in choice-reaction step times. Such an approach could be applied to the current paradigm to gain sensitive measures of weight shifting and stepping errors.

This new method builds from an established reactive balance test where participants are released from a supported lean, and now includes scenarios that demand behavioral flexibility. Test designs suitable for exposing response inhibition and action selection allow us a way to apply concepts from cognitive psychology to the domain of balance control. Such an approach is necessary to build upon the recognition that cognitive decline and fall prevalence are correlated, and to gain a mechanistic understanding for how cognitive resources prevent falls. Presumably this setup could be used not only as a research tool, but also as a means for training cognitive roles in balance. An important aim of ongoing work our laboratory is to understand how the brain utilizes contextual information to update which movement would be most suitable to prevent a fall given the surroundings. Cues such as the availability of a stable handhold or a potential step barrier can guide which response to make should the need arise and may covertly shape predictive brain processes¹⁶. Notably, the capacity to appropriately use this information may deteriorate with age if mental faculties such as inhibitory interference control or visual-spatial memory are required. Given the relationship between cognitive decline and falls¹⁻³, implementing study designs that emphasize a need for integrating contextual relevance could provide valuable insight into balance deficits in many vulnerable populations.

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DISCLOSURES:

The authors have nothing to disclose.

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Figure 1

[Click here to access/download;Figure;JoVE_Figure1.jpg](#)



Figure 2

[Click here to access/download;Figure;JoVE_Figure2.jpg](#)

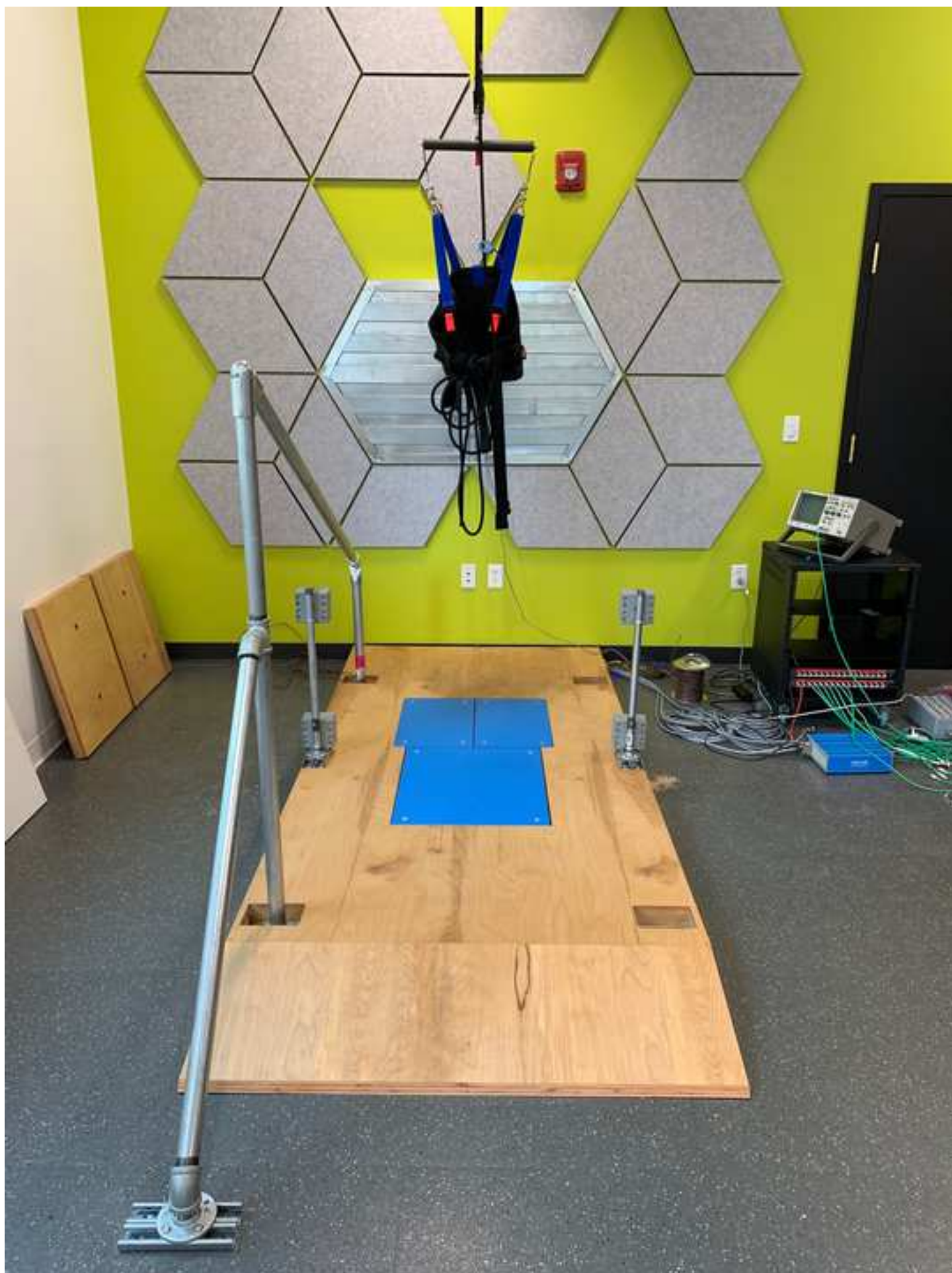
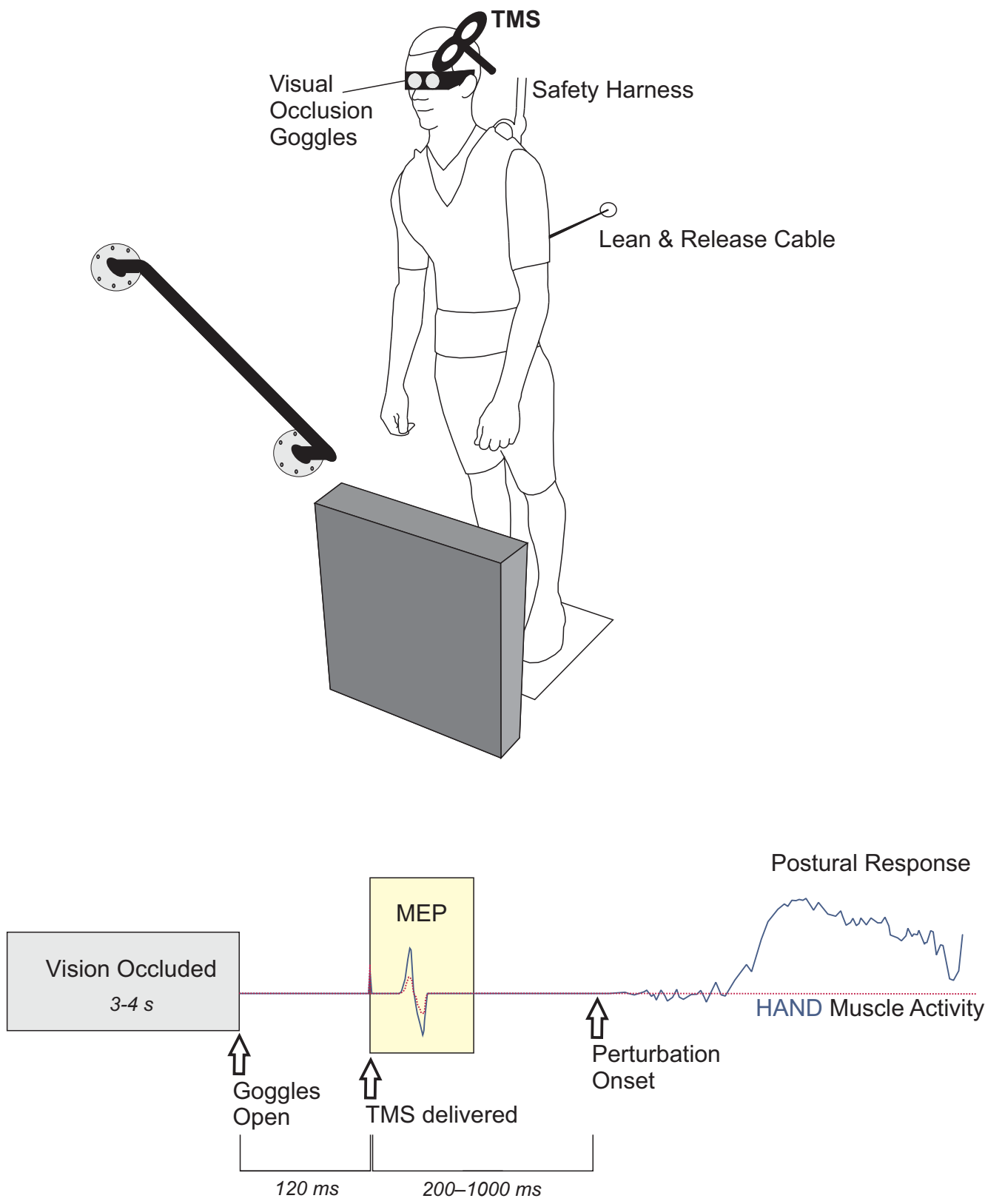


Figure 3



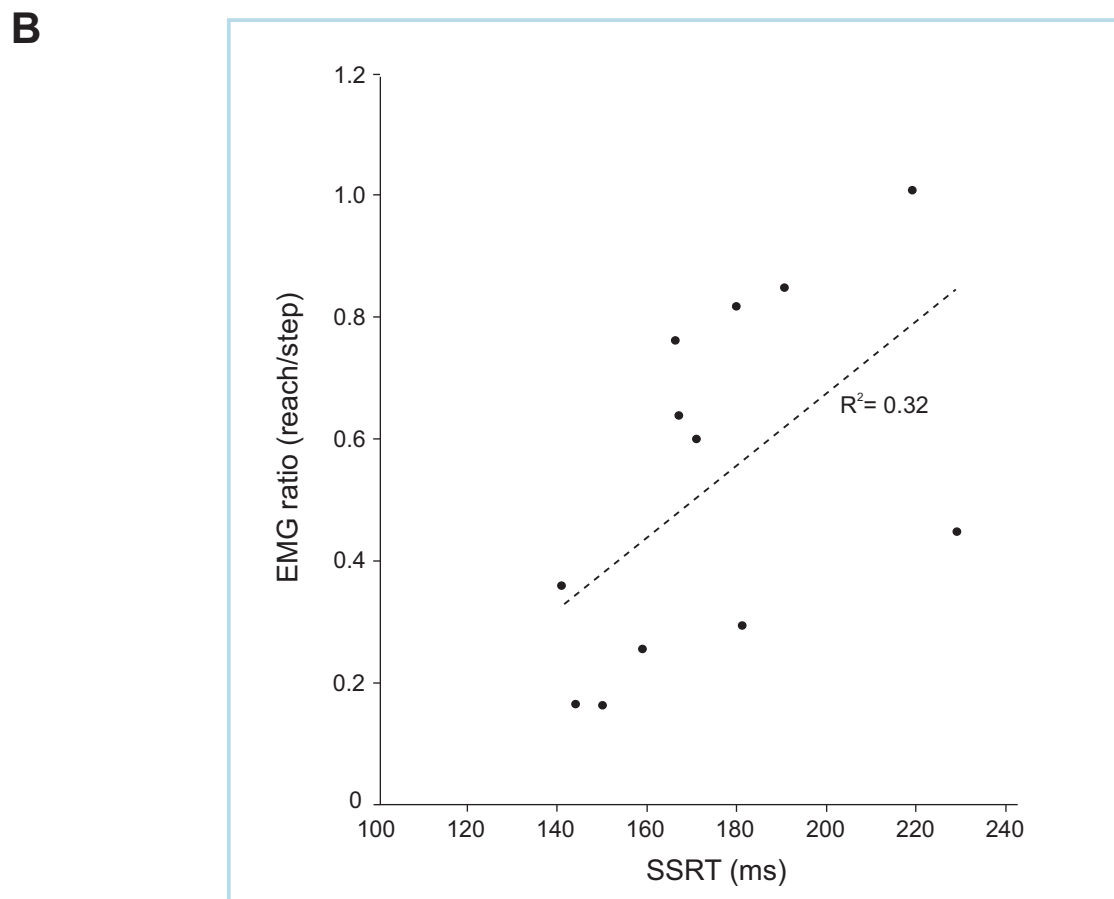
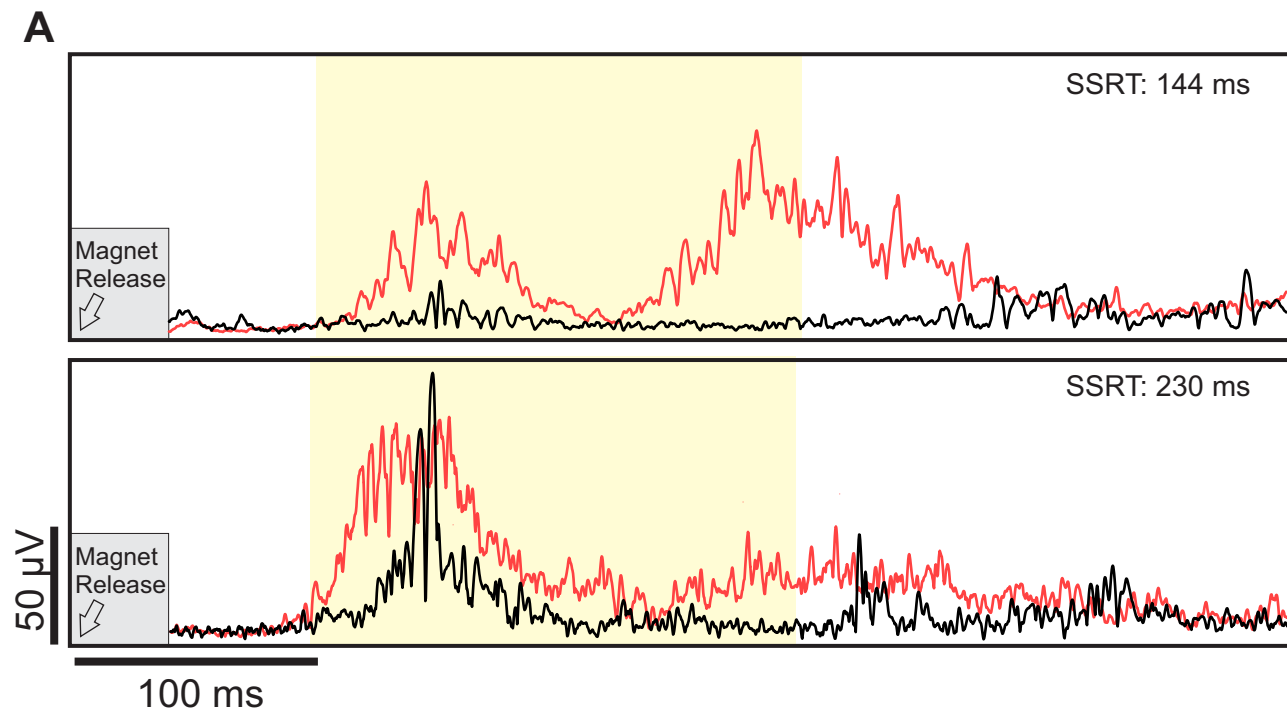
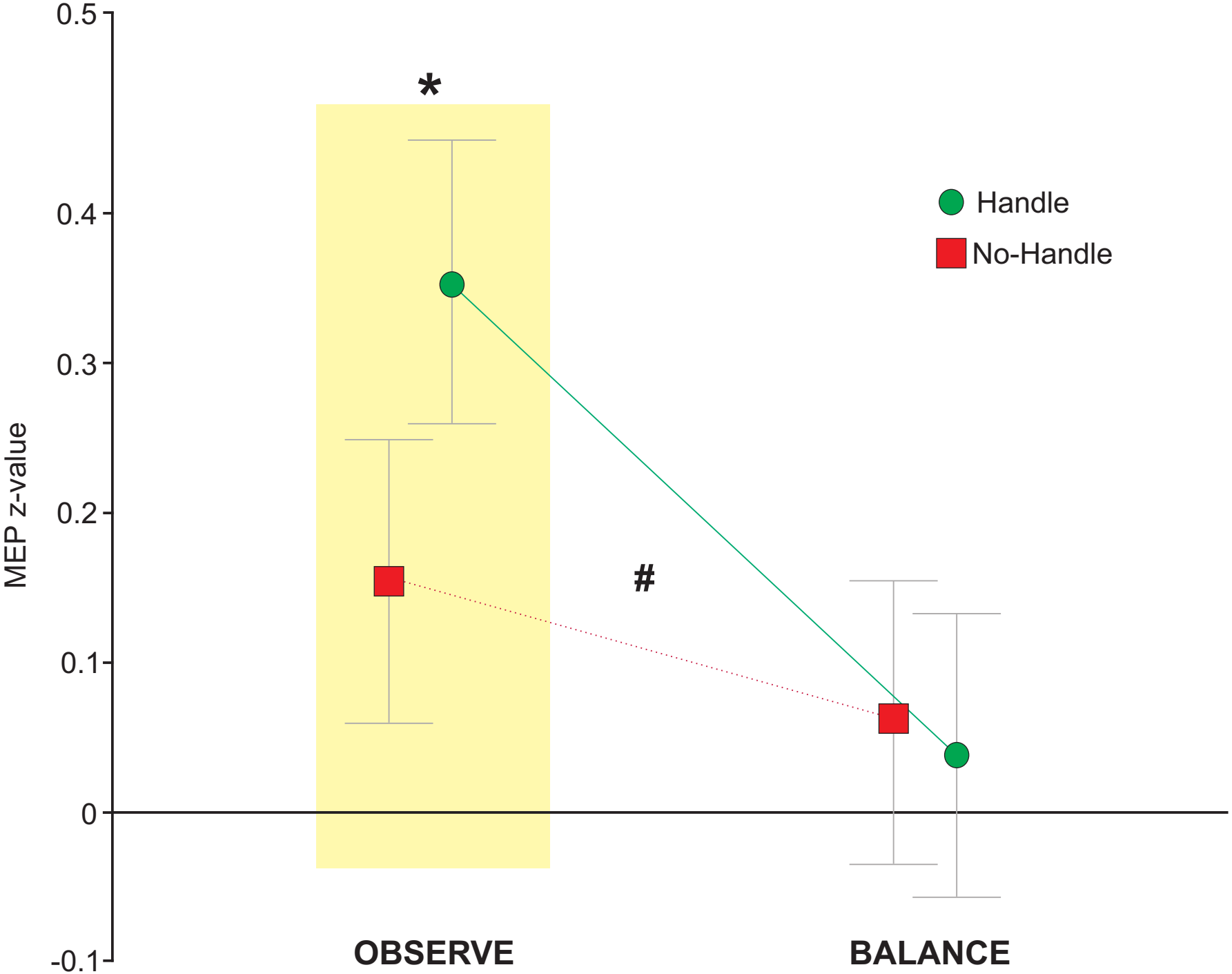
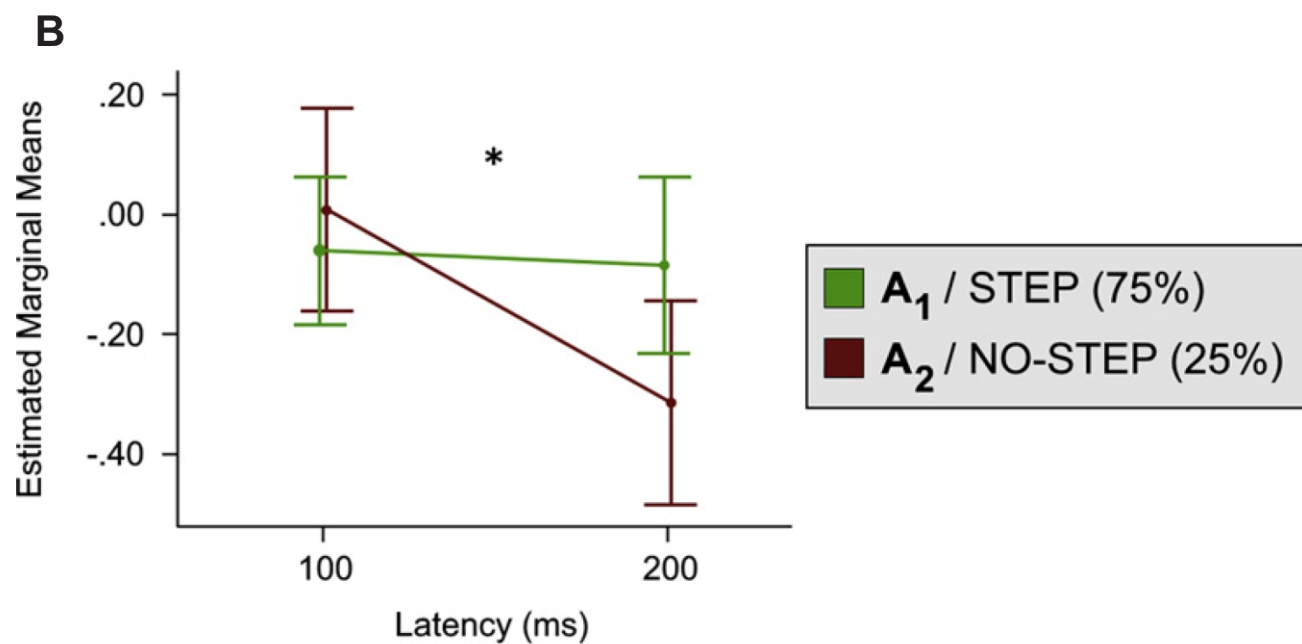
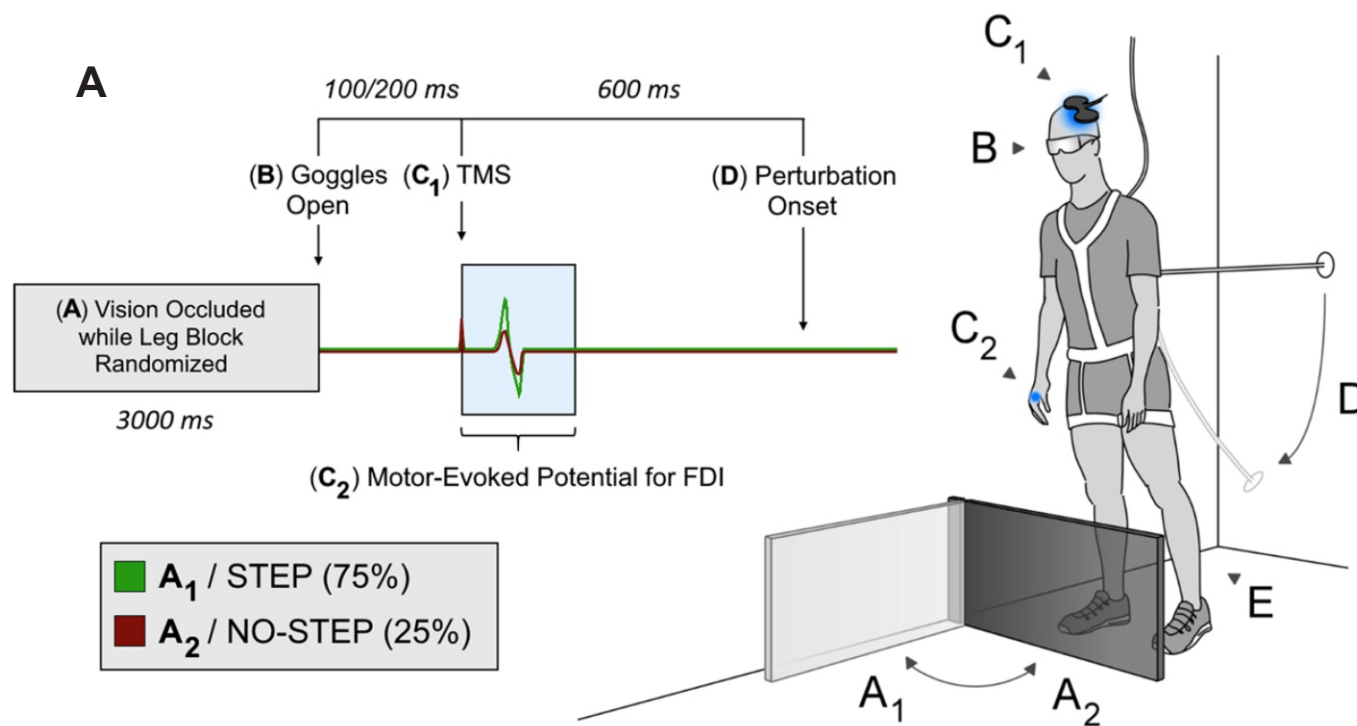


Figure 5





Name of Material/Equipment	Company	Catalog Number
CED Power1401	Cambridge Electronic Design	
Delsys Bagnoli-4 amplifier	Delsys	
Figure-eight D70 ² Coil	Magstim Company Ltd	
Kistler Force Plates	Kistler Instrument Corp.	Multicomponent Force Plate Type 9260AA
Magstim 200 stimulator	Magstim Company Ltd	
PLATO occlusion spectacles	Translucent Technologies Inc	
Signal software	Cambridge Electronic Design	Version 7

Comments/Description

Data acquisition interface

EMG equipment

TMS coil

Force plates

TMS stimulation units

visual occlusion

Response to reviewers

Ms. No. JoVE60688

Title: *A modified lean and release technique to emphasize response inhibition and action selection in reactive balance.*

Response to Reviewers

We are grateful for the time and effort committed by the editor and reviewers in critically evaluating our manuscript. Our responses to the concerns and questions are presented below. In the present document, reviewer and editor comments are in italicized Helvetica font. Our responses are shown in Times New Roman font. Revised sections of the manuscript are in red font.

Editorial comments:

General:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.
2. Please print and sign the attached Author License Agreement (ALA). Please then scan and upload the signed ALA with the manuscript files to your Editorial Manager account.
3. Please revise lines 65-70, 132-136, 192-222, 236-255, and 271-314 to avoid textual overlap with previous results.
4. The 'Appendix' mentioned in the Discussion was not included in the current submission.
5. JoVE cannot publish manuscripts containing commercial language. This includes trademark symbols (™), registered symbols (®), and company names before an instrument or reagent. Please limit the use of commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials and Reagents.
For example: Delsys, Bagnoli-4, M-wrap

Response: We have now addressed each of these points as instructed. In particular, we have attached our signed Author License Agreement, included the Appendix, and revised the sections in the manuscript noted above.

Protocol:

1. Please ensure that the protocol is largely written in the imperative.
2. Please include no more than 2-3 actions and 4 sentences per numbered step/substep.
3. For each protocol step/substep, please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. If revisions cause a step to have more than 2-3 actions and 4 sentences per step, please split into separate steps or substeps.

Response: We have now addressed each of these points as instructed.

Figures:

1. Please obtain explicit copyright permission to reuse any figures from a previous publication. Explicit permission can be expressed in the form of a letter from the editor or a link to the editorial policy that allows re-prints. Please upload this information as a .doc or .docx file to your Editorial Manager account.
2. Please include a space between numbers and their corresponding units (e.g., “120 ms”). Please use ‘ μ ’ instead of ‘u’.

Response: The evidence for copyright permission has now been provided. Please see attached. Also, the spaces have now been added between numbers and their units.

Table of Materials:

1. Please ensure the Table of Materials has information on all materials and equipment used, especially those mentioned in the Protocol.

Response: The revised Table of Materials provides information on all materials and equipment outlined below.

Reviewer #1:

Manuscript Summary:

This manuscript is concerned with presenting the possibility of a new way of assessing reactive balance actions. It is novel in its methods, providing a clear argument regarding why it is needed. The introduction highlights other techniques shortcomings, specifically, how current methods do not challenge the postural control system in a manner such as what the authors propose. It was an enjoyable read, given the clarity they used throughout the manuscript. The discussion provides good insight into the limitations of the proposed system. I feel the work is worthwhile and has the potential to produce some exciting new studies in the area of postural control. I have some minor comments that the authors should think about below, they are mainly situated around the protocol.

Response: Thank you for your comment.

Minor Concerns:

Minor point 1: Line 162: 3.1.2. The cable is released at unpredictable intervals. How is this accomplished? Is this done by the researcher or by a computer generated sequence? Some research uses predictable perturbations and compares them to an unpredictable perturbation, can this be accomplished? This detail would aid in the description of this section.

Response: The timing of cable release is controlled by computer commands pre-set into our main acquisition program (created using Signal software, which is a software designed to work with our CED Power1401 data acquisition system). These programs are written to use specific

‘states’ that determine precisely when the cable is released during a particular trial. For example, (a) cable release 200 ms after the goggles open might be labelled state 1, (b) cable release 400 ms after the goggles open, might be state 2, and so forth. These states are then programmed to cycle in a random fashion. In this way, experimental control over cable release is accomplished through a computer program with a randomization setting. We have now revised the manuscript to include the following statement:

“The precise timing of cable release is controlled via computer commands, pre-set into a *Signal* configuration. This configuration allows us to control timing of cable release so that it can be randomized across trials.”

As noted by the reviewer, studies into reactive balance control often manipulate the predictability of perturbation onset. This option is available using our system and it would require only minor changes in the *Signal* program to deliver blocked trials of a constant perturbation onset (instead of randomized trials). We have now included a comment in the revised manuscript to address this option. Thank for you this suggestion.

“NOTE: The *Signal* configuration that controls all experimental devices (e.g. triggering the motor to position a leg block) sets the specific trial condition (e.g. if a leg block is present or not). This can be programmed to randomize conditions or deliver them in blocks to control the level of predictability.”

Minor point 2: *I notice that it is mentioned in the next section (3.1.3) that the experimenter has the ability to release the cable. Seems odd to place it here when you have mentioned it in the above section. I think it would be clearer to state this in the previous section as it is concerned with the release of the cable. Or maybe 3.1.2 just needs deleting? As the information seems to appear throughout the differing sections.*

Response: We have now deleted the redundant comment (originally *subsection 3.1.2.*) as recommended and revised *section 3* to present this information more logically.

Minor point 3: *Line 172: "handing"... hanging?*

Response: We have revised this to read as ‘*hanging*’.

Minor point 4: *Line 173: I know it is common practice to have a safety harness, obviously it is warranted due to the injury risk of such studies. I think, however, it needs to be clear that the harness will not support any bodyweight until it is absolutely necessary.*

Response: We agree this point needs to be made more clearly. We have now included the following sentence in the revised manuscript:

Response to reviewers

“It should be noted that this failsafe cable provides no bodyweight support until absolutely necessary (i.e. if a participant is unable to recover balance on their own and the cable ‘catches’ them before falling to the ground).”

Minor point 5: *Line 178: "gaze fixation is standardised" ... how? (Mentioned in 4.3, suggest stating earlier at this position instead).*

Response: We have now moved the point from *section 4.3* on setting of gaze to earlier in the methods as suggested by the reviewer. The new *subsection 3.1.5* now reads as follows:

“Due to the importance of reliable visual information, it is essential to verify with participants that they can actually see the handle and leg block when wearing the goggles. Each trial begins with participants instructed to look directly at a fixation point on the floor, about 3 metres in front of them, while holding their head in a comfortable position. Participants are positioned such that gaze is set to view the handle in the peripheral visual field and the top portion of the obstacle.”

Minor point 6: *Regarding the leg blocks. The current version should work well for the intended purpose (i.e. blocking the step reaction to force the grasp). I do wonder, however, if the authors considered introducing a smaller version of the blockade that could act as a fake potential trip hazard, requiring participants to step over. This could be used in conjunction with the handle or even without. This could provide vital information regarding postural responses to obstacle avoidance.*

Response: This is an interesting suggestion, and one that could be built into our system with minor renovations. In our current model we have two motors controlling each leg block – one at the top end of the support bar, and one at the bottom. To make the modification suggested by the reviewer it would be straightforward to simply attach a smaller/shorter obstacle to the lower motor. Each motor has sufficient capacity to move such obstacles. The use of a shortened leg block could in theory pose a more graded threat to a recovery step where participants could step over the obstacle as opposed to our current arrangement that involves an ‘all-or-none’ type decision. We have now included the following sentence in the revised manuscript:

“NOTE: The leg blocks have been constructed to force an ‘all-or-none’ step decision given that they rise almost 30 inches off the ground (mid-thigh level on most individuals). For researchers interested in a more nuanced blockade of a recovery step, our device could be modified to use a smaller/shorter obstacle which would then allow an adapted step to clear this obstacle.”

Minor point 7: *Line 226: 4.1 do the authors recommend a minimum/maximum amount of trials for familiarization? May there be a need for a longer period? Have the authors observed any evidence of participants getting better at the task after X amount of trials before plateauing?*

Response: From our experience the number of trials required by any given participant tends to vary, and anecdotally this seems to take a few more trials for the older adults versus younger adults. In our approach we familiarize participants first with recovery steps (~2-3 attempts), then grasping (~2-3 attempts) and finally expose them to both conditions at random (~3-5 attempts). On average, participants require approximately 10 practice attempts (we have now included this point in the revised manuscript for *section 4.1*). Our main purpose for the practice is to get participants familiar with the fact that they need to execute one of two different actions. Through observation and speaking with the participant during practice we will make gauge if they fully understand the task, and determine their readiness to start with regular testing. Thus far we haven't tracked a learning curve, at least using formal analysis.

Minor point 8: *Having not used TMS myself, I would not like to comment greatly on its suggested application. I merely wish to state that based on my knowledge and reading of the tool, the protocol appears to be accurate.*

Response: Thank you for your comment.

Minor point 9: *Line 335: An R^2 value of 0.32 is small and should be reported as such here. In the examples how many trials were used for data collection?*

Response: For this study by Rydalch et al, 2019, each participant performed 256 trials where 70% of the trials allowed a stepping response, while 30% of the trials blocked a step, but allowed a grasping response. The manuscript has been revised to include the following sentence:

“In the balance task a total of 256 trials were collected, of which 30% used a leg block.”

We have also revised the manuscript to state that our reported R^2 value is classified as small:

“The scatterplot in Figure 4b depicts a small, but significant correlation between the ability to suppress a blocked step and response inhibition as measured by the stop-signal reaction time.”

Reviewer #2:

Manuscript Summary:

This purpose of this manuscript is to outline a method for examining reactive responses when balance perturbations are induced in the forward direction by a lean and release method. The authors cited that the current methods have limitations because previous literature only

examines the reflexive responses of timing and do not examine cognitive processes. Furthermore, the timing of balance recovery is not important. Other studies use the timing of the responses which is a limitation of the current method used to study falls.

Major Concerns:

Point 1: *I find the paper poorly organized and difficult to follow. The purpose of the study is not supported by the methods. The purpose of the study is doing the right thing at the right time rather than how fast a person can recover from an external balance perturbation although the authors' purpose incorporates a timing component, so they believe that the timing of the is important. Even though the authors suggested that only examining the timing of the reaction response is the limitation of other studies. I am not sure there is a right thing to do, but rather a person will do what they are capable of doing within the allotted time that they have to respond before falling.*

Response: We agree that speed is essential when generating a compensatory balance response to prevent a fall. In presenting our modified lean and release method we do not claim that timing is unimportant in balance recovery. Rather, we stress that additional cognitive factors, such as inhibitory control and/or the ability to select appropriate action, are also important in certain situations. Some reactions are optimal in a given situation to avoid a fall, while other reactions can lead to further instability. Unfortunately, these factors are often neglected in balance assessment. In many of the complex settings we face in everyday life there may be multiple options to select from when choosing a specific recovery action (e.g. grasping a nearby support rail instead of stepping) and in some circumstances, suppressing a highly automatic action may be important (e.g. avoid stepping into a pothole or an obstacle). It is this contextual relevance we wish to emphasize. In our view, both response speed and appropriateness of action are necessary to prevent a fall when faced with a complex, choice-demanding setting.

The *Introduction* has now been revised to avoid any implication that speed of response is not important, thus we have removed the following sentence: “This study emphasizes ‘doing the right thing at the right time’ rather than how fast a recovery step and/or reach takes place, in contrast to traditional approaches for assessing balance (e.g. speed and magnitude of muscle response).”

Furthermore, we have added the following sentence to the first paragraph of the *Introduction*:

“While factors such as response speed are essential to prevent a fall, additional cognitive factors, such as inhibitory control and/or the ability to select appropriate action based on a given context may also be important in certain situations.”

Point 2: *It is not clear what cognitive processes the authors are examining in this study. Perhaps the decision making is what is considered a cognitive process. Is this part of the motor preparation? Data on what method of recovery chosen would provide support for decision making or did the participants make the same decision. I would not constitute decision making as a cognitive process. From the time of the perturbation to the onset of the muscle activity this is approximately 100 ms before the EMG activity is initiated, do you think that it is possible to make a decision in 100 ms in addition to visually processing the environment.*

Response: While cognition encompasses a wide range of mental abilities, a common view of cognitive function refers to multiple mental abilities, which includes memory, problem solving, attention, and decision making among others.

As an example, Newen (2017)¹ integrated the many ways in which cognition has been framed, and this includes decision making as part of cognitive processing: “*Cognitive processes are processes of information transfer that typically take place to connect multiple (or complex) informational inputs to form a minimally flexible cognitive system with a spectrum of minimally flexible behavioral outputs, where these processes typically involve (at least a minimal level of) one of the following paradigmatic processes as described in certain cognitive sciences with a cognitive method: perception, memory, learning, emotion, intentionality, self-representation, rationality, and decision-making or something relevantly similar to it.*”

Also, Gold & Shadlen (2007)², in their review include decisions as a hallmark of higher cognition. As part of their comprehensive review they state: “*A decision is a process that weighs priors, evidence, and value to generate a commitment to a categorical proposition intended to achieve particular goals.*”

With our method, decision-making is emphasized because participants are required to decide amongst two options: (a) step/don't reach or (b) reach/don't step. Traditional cognitive neuroscience studies usually rely on simple button presses to measure decision-making, whereas the decision using our approach is measured by compensatory stepping and/or reaching responses. In addition to our emphasis on decision-making (i.e. which action to select in our study), we stress a need for response inhibition. Response inhibition is a hallmark of executive function³ where automatic response tendencies are overridden to revise behaviour, therefore this is a foundation for behavioural flexibility. For present purposes, both inhibitory control and the ability to appropriately select a response are required to be successful in our modified lean and release task.

To address the reviewer's next point on motor preparation related to cognitive processing and decision making, we use TMS to investigate visual priming of muscle representations. This method provides insight into motor activation triggered by viewing an object, which in this case is an object associated with stability (support handle). While this priming effect not a 'decision' per se, it does represent a cortical-based mechanism that links vision of our surrounding environment to potential action. This idea of 'affordances' was originated by Gibson (1979)⁴ who proposed that we perceive the world in terms of behavioural value. In motor terms, this means the potential action(s) the object affords. Many researchers since Gibson have shown neurophysiological evidence for this effect⁵⁻⁹. Recent work by Freeman et al (2016)¹⁰, suggests that the affordance effect (in seated participants using EEG) is actually abolished during a cognitive-demanding task and the authors proposed that this indicates the affordance effect may rely on cognitive resources. This suggests that the affordance priming we found relies on cognitive resources to link what is viewed with its associated action(s).

Beyond visual priming, we quantify response inhibition and decision-making more directly in the leg responses to a perturbation. Specifically, we measure muscle activity in the legs to gauge

a tendency to respond in a situation where a response should be suppressed. For example, in the Rydahl et al, 2019 study, we looked at the response magnitude in an ankle dorsiflexor of the stepping leg when participants were released from the support cable. In this situation, participants needed to either step forward to regain balance, or if a leg block was present they needed to refrain from stepping and grasp the handle instead. To accomplish this, the integrated EMG was measured between 100-300 ms after cable release and used to calculate a muscle response ratio (reach/step iEMG). Here, we tested the ability of participants to suppress an automatic balance recovery step when a leg block was present using a sensitive measure of muscle activity.

To address the reviewer's final point here, it is important to highlight that decision making in these studies is not limited to the onset of perturbation. Instead, we provide visual access to the response environment before cable release. Although the allotted time between vision and release is brief, we normally provide vision of the scene for at least 200ms before the release.

References:

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2. Gold, J and Shadlen, M. (2007). The Neural Basis of Decision Making. *Annual Review of Neuroscience* 30:1, 535-574.
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8. Makris et al. (2013). Are object affordances fully automatic? A case of covert attention. *Behavioral Neuroscience*, 127(5), 797–802.
9. Makris, S., Hadar, A. A., & Yarrow, K. (2011). Viewing objects and planning actions: on the potentiation of grasping behaviours by visual objects. *Brain and Cognition*, 77(2), 257–264.
10. Freeman, S. M., Itthipuripat, S., & Aron, A. R. (2016). High Working Memory Load Increases Intracortical Inhibition in Primary Motor Cortex and Diminishes the Motor Affordance Effect. *Journal of Neuroscience*, 36(20), 5544–5555.

Point 3: *There is a multitude of factors that are included in the experimental design which are not clearly outlined, for example the SSRT. There is no explanation of what this task involved to understand the purpose and what the correlation means in Figure4.*

Response: We agree that adding more information on this cognitive task is warranted. We now include a brief outline of this task (stop signal task) in an *Appendix* within the revised manuscript. The outline reads as follows:

“In the SST, the participant is repeatedly exposed to a ‘go’ cue and asked to quickly press a button on a keyboard. Occasionally, a stop signal follows the go cue, indicating that the participant should withhold action. The SST is designed to estimate the stopping process by manipulating specific variables in a performance tracking algorithm. A race ensues between two independent mental processes - a go, and a stop process – and this model

provides theoretically justified estimates of the latency of stopping¹. Such estimation is necessary given the unobservable latency of the stopping process. Our SST program was custom written in Matlab (Mathworks, MA), adapted from a version used by Aron & Poldrack². This test is completed while participants sit at a desk facing a computer. They will be presented with a go signal (“<” or “>”) and instructed to respond as quickly as possible by pressing the appropriate button on the keyboard (i.e. press “>” if the arrow points right, and “<” if the arrow points left). They will be asked to do this as quickly as possible once the arrow appears, but to refrain from responding if a stop tone is heard. On 25% of the trials, the stop signal follows the go cue at random. The delay between go and stop signals is referred to as the stop-signal delay. The basic idea is that inhibition of the prepotent response is more difficult when the inhibitory stimulus is presented after a longer time interval than a shorter one. When the stop signal is presented close to the go stimulus onset, a response is easier to inhibit however, as the onset of response execution approaches, stopping becomes increasingly difficult. Because the actual latency of the stopping process cannot be directly measured it must be estimated from a stochastic model, and in this way the covert stopping process (SSRT) is estimated. The stop-signal delay is varied to yield a 50% probability of correctly inhibiting a go response after a tone. The delay where participants inhibit their reaction 50% of the time, is used to estimate the SSRT.

References for Appendix:

1. F. Verbruggen, G.D. Logan, Models of response inhibition in the stop-signal and stop-change paradigms, *Neurosci. Biobehav. Rev.* 33 (2009) 647–661.
2. A.R. Aron, R.A. Poldrack, Cortical and subcortical contributions to Stop signal response inhibition: role of the subthalamic nucleus, *J. Neurosci.* 26 (2006) 2424–2433.”

In addition to describing the Stop signal task (SST) in the *Appendix*, we now provide an explanation for why the correlation between the outcome measure of the SST – the stop signal reaction time, or SSRT - and muscle response ratio is important. The revised manuscript reads as follows:

“When interpreting these results, it is important to recognize that the SST (described in the *Appendix*), and indeed most cognitive tests, rely on simplistic responses (often finger movements) made by seated participants in response to imperative cues displayed on a computer screen. This study by Rydalch et al, (2019) addressed if the ability to stop a prepotent response was preserved across a standard seated test of response inhibition compared with a reactive balance test where compensatory steps must be occasionally suppressed. The results showed a correlation between the cognitive test outcome (stop signal reaction time) and compensatory stepping, which suggests that an individual’s stopping capacity generalizes across diverse tasks.”

Point 4: *If the authors measure motor preparation than it is not clear why the stimulation of the brain was between the google opening and the external perturbation to balance. At this time point, individuals would not be preparing for a movement because they have been told not to prepare until there is a perturbation to balance. The change in MEP in this time period would be*

the change in visual input when the googles are opened. Unless individuals are cued with a warning light and informed when they see this warning light to prepare for a movement there is no reason to preplan a movement.

Response: It is correct that individuals would not be preparing for movement when the TMS pulse is delivered. In fact, it is important for our purposes that they are relaxed at this time. Our rationale for delivering TMS after vision, but before movement is to determine how viewing an object by itself will impact motor activity. Described above (response to Point 2), our approach is based on the concept of affordances where it is proposed that we perceive objects in terms of behavioural value (i.e. put them into potential motor terms when simply observing them). Our approach is to use TMS as a ‘snapshot’ into how the brain translates the viewed object into potential motor terms. The key example from our work is that viewing a wall-mounted support handle resulted in facilitation of intrinsic hand muscles within 120ms of viewing the handle. This occurs even in a setting where no action is required (both in seated and standing conditions). There is never an intention to move and therefore no reason to plan action. This shows that viewing an object such as a handrail by itself conjures the relevant hand muscles for grasping (a covert preparatory mechanism). Given that facilitation results from viewing a supportive handrail, we speculate that such priming has implications for aiding a grasp onto a handrail should an unexpected perturbation occur.

Minor Concerns:

Minor Point 1: *Lines 52-53. The authors state we, "fail to understand the brain's role in reactive balance is due to research protocols currently in use." There needs to be a citation for the currently used research protocols.*

Response: We agree with the reviewer that we should offer more support for our claim. In response, we now include the following new paragraph in the revised *Introduction*:

“Rogers and Mille (2018) recently summarized the different ways in which balance control has been assessed using external perturbation. These methods include platform translation, tilts and/or drops, as well as the use of automated systems that push, pull or remove postural support. Despite the large variety of techniques used to disrupt upright equilibrium, the ensuing corrective reactions are almost always made in an unobstructed environment, thus minimizing constraints on movement.”

Minor Point 2: *Lines 108-109, the lean and release method is not a novel method for inducing balance reactions. This method has existed for many years with an extensive publication list.*

Response: We acknowledge that the lean and release method has been used for many years. The innovation with our *modified* lean and release approach is that we manipulate the setting in front of a participant while controlling access to vision. By altering the surrounding environment, we force a need for response inhibition and action selection during balance recovery. Typical lean & release studies do not require inhibitory control or action selection, but instead focus on a pure rapid stepping reaction to recover balance. For examples see references listed below.

References:

Response to reviewers

1. G. Mochizuki, S. Boe, A. Marlin, W.E. McIlroy, Perturbation-evoked cortical activity reflects both the context and consequence of postural instability, *Neuroscience*. 170 (2010) 599–609.
2. D.G. Thelen, M. Muriuki, J. James, A.B. Schultz, J.A. Ashton-Miller, N.B. Alexander, Muscle activities used by young and old adults when stepping to regain balance during a forward fall, *J. Electromyogr. Kinesiol.* 10 (2000) 93–101.
3. L.A. Wojcik, D.G. Thelen, A.B. Schultz, J.A. Ashton-Miller, N.B. Alexander, Age and Gender Differences in Single-Step Recovery From a Forward Fall, *J. Gerontol. Ser. A*. 54 (1999) M44–M50.

Minor Point 3: *How was the angle of the lean determined for each person? What test was performed that would ensure a change in the base of support would be needed each time the cable was released?*

Response: Once each participant was set up in the harness and attached to the failsafe cable (i.e. ceiling cable) we would then attach the second cable to a magnet fixed to the wall. We typically started at a lean angle of ~10 degrees and then released the participant. For the initial practice trials, participants were always instructed to take a rapid step to regain balance. We then lessened the lean angle incrementally to a point where participants were just barely able to recover upright stability without resorting to a forward step. We then set the lean angle to slightly steeper than this threshold point to ensure the participant would need to step to recover balance. Following this process, participants were instructed to step quickly to recover balance unless the leg was blocked. *Note: for the Goode et al, 2019 study we actually selected a lean angle where a fixed support was just feasible.*

We have added the following information to our new *subsection 3.1.7*:

“The specific lean position is determined as the minimal lean angle where a forward step is necessary to recover balance when the cable is released. This is an iterative process to find a threshold lean angle at the ankle joint, which is the angle where the participant is no longer able to prevent a forward fall using a feet-in-place reaction. Once this is established, the lean angle can be verified throughout testing using goniometry.”

Minor Point 4: *How many participants participated in the study? And the general characteristics of the population would be helpful, ex age, sex, etc.*

Response: We have now added the following statement to address this point in our revised manuscript, as a preface in the *Representative Results* section:

“Note: All exemplar studies presented below were conducted with young women and men between 18-30 years of age. Total sample size for each study was as follows: Example 1 (Rydalch et al, 2019) included 12 participants, Example 2 (Bolton et al, 2019) included 63 participants, and Example 3 (Goode et al, 2019) included 19 participants. The reader should refer to the complete studies for details on methods and analysis.”

Minor Point 5: *Under 4.5, the authors state that there is a delay in the release between 100-1000, is this after the googles have been opened to allow for vision.*

Response: Yes, there is a delay ranging from 200ms to 1000ms after the goggles open. We have now revised this section to state this more clearly. Specifically, the revised text now reads:

“On trials where a perturbation does occur, the cable releases shortly after the goggles open. This delay period varies with study requirements, but ranges from 200-1000 ms.”

Minor Point 6: *Line 275, the TMS was delivered after vision introduced, what do the authors mean by "a short time." Was this a variable time or a fixed time? Why did the authors choose to examine the motor preparation of the hand and not dorsiflexors during stepping? The first part of the paragraph states that the TMS is time located to the opening of the goggles. The timing of the TMS relative to the introduction of visual input. Either the TMS could be aligned with the initial processing of the visual stimulation which would precede the motor preparation. 5-1 and 5-6 should exist in the same paragraph since they are both related to timing.*

Response: The timing of TMS pulses is something we purposely manipulated and the specific timing for TMS delivery was slightly different for each study depending on the research question. For example, in our representative result from Bolton et al, (2019), TMS was always delivered 120ms after the goggles opened. The rationale for this specific timing was based on a preliminary study (McDannald et al, 2018¹) where we revealed facilitation of intrinsic hand muscles when TMS was delivered 120 ms following visual access to a support handle (i.e. the affordance effect described earlier). For the representative result by Goode et al, (2019) we delivered TMS at two different points following vision - 100 ms and 200 ms - to determine if suppression was evident in a task-irrelevant hand muscle. This was premised on work by other researchers (e.g. Majid et al, 2012²) who have shown that rapid cancellation of action results in widespread inhibition throughout the motor system – a concept known as *global suppression*. Also, we agree with the reviewer that subsections 5.1 and 5.6 would be more suitably presented together. Section 5 has now been rewritten and condensed into 4 subsections (down from 6).

References:

1. D.W. McDannald, M. Mansour, G. Rydalch, D.A.E. Bolton, Motor affordance for grasping a safety handle, *Neurosci. Lett.* 683 (2018) 131–137.
2. D.S.A. Majid, W. Cai, J.S. George, F. Verbruggen, A.R. Aron, Transcranial Magnetic Stimulation Reveals Dissociable Mechanisms for Global Versus Selective Corticomotor Suppression Underlying the Stopping of Action, *Cereb. Cortex.* 22 (2012) 363–371.

Minor Point 7: *Line 322, the line has listed ref. Is there a reference for this statement?*

Response: Thank you for catching this oversight. The appropriate reference (Rydalch et al, 2019) has now been added.

Minor Point 8: *The authors mention a task, stop-signal task (line 331), which was not explained in their methods. It is unclear how this part of the experiment was carried out. Also, the purpose of the comparison is not clear.*

Response: This was the seated cognitive task (Stop signal task) we used to compare with compensatory stepping reactions. We have now included an explanation of this task in the revised manuscript (see new *Appendix*). We also provide a rationale for using this task to compare with a corrective balance reaction under *Representative Results*. Please see our more detailed response to point 3 above.

Minor Point 9: *It is unclear the authors ensured the participants would be preparing for a movement. What instructions were the participants given to ensure that they were planning for a movement. Typically studies that examine motor preparation give instructions to the participant after a warning to preparation to move at a go signal.*

Response: The specific instructions varied slightly for each study, but for all studies participants were instructed to remain relaxed unless prompted to recover balance by cable release. This is written in our revised *subsection 4.1*.

“Throughout testing and practice the participants are instructed to remain relaxed unless prompted to move by a sudden cable release.”

Our goal was to investigate how corticospinal excitability was affected by viewing objects in the environment (e.g. handle). Although some preparation may have inadvertently taken place, we did take steps to control for this by excluding any data from analysis where participants activated muscles before cable release. For brevity, we refer the reader to the original journal articles for these details and include a brief sentence at the beginning of the *Representative Results* section as follows:

“The reader should refer to the complete studies for details on methods and analysis.”

Minor Point 10: *What is the justification for measuring the MEP of the muscles in the hand and not in the leg? You had not measured any motor preparation for stepping responses or suppression of stepping responses when the leg was blocked.*

Response: Our main research questions thus far have focused on hand muscle activity in response to visual cues that either afford or obstruct action. Previous research into this topic of affordances for action used TMS to reveal this effect in seated individuals while they viewed graspable objects on a computer screen (e.g. coffee mugs with a handle oriented either toward or away from the target hand*). As our initial foray into this area, the hand seemed like a reasonable target to determine if visual priming was evident in a standing subject when they viewed a support handle. Similarly, in the Goode et al, (2019) study where we explored global suppression as it pertains to reactive balance, we were interested in how a task-irrelevant muscle was impacted by a need to suppress a step. Again, the hand represented a logical first target. From a practical standpoint, TMS delivered to a hand target is far easier when isolating a motor hotspot and requires lower stimulation intensities, which makes data collections considerably more comfortable for the research participants. That said, we agree with the reviewer that leg muscle activity would offer a valuable measure. At this stage, we have established basic methods

to combine TMS with our lean and release set-up, and we plan to assess leg muscles in future work.

Reference:

*Buccino, G., Sato, M., Cattaneo, L., Rodà, F., & Riggio, L. (2009). Broken affordances, broken objects: A TMS study. *Neuropsychologia*, 47(14), 3074–3078.

Reviewer #3:

Manuscript Summary:

This manuscript is well written, and describes a protocol and construct which can provide insights into an important aspect of movement, choice, and awareness/context during quick postural control.

Response: Thank you for your comment.

Major Concerns:

Point 1: *Authors note (e.g. line 455) that leaning has some inherent limitations to other types of unknown perturbations such as waist-pulls or support surface movement. It may be worth adding 1-2 additional sentences to expand on these limitations. One example is that participants are acutely aware of the magnitude of perturbation that will be received (in that their own lean/weight will produce this perturbation. Further, that the direction is known, the lower limb muscles that would be recruited could be primed for activity and it is unlikely (although possible) that antagonistic lower limb activation would occur.*

Response: Thank you for the suggestion. We have revised our *Discussion* to include the following information:

“The proposed method has potential to provide a unique glimpse into the neural control of balance, but poses certain limitations. For example, when using the lean and release method, the cable release is initiated from a forward lean which necessitates a pronounced balance recovery step compared with other methods of external postural perturbation. Also, the direction and magnitude of the perturbation are predictable, which again represents a limitation with this approach. This is particularly true since predictability may lead to anticipatory activation of muscles that would normally not be engaged in more realistic fall scenarios. Finally, vision is temporarily occluded prior to cable release, which also deviates from our regular experience of the world.”

Point 2: *Considerable emphasis is placed on demonstrating whether the correct motion occurs (i.e. the choice between the hand movement or step), however little detail is provided regarding quantification of this movement (accuracy of hand movement, size or efficiency of step, etc.).*

Response: This is an excellent point, and something our research group has only partially addressed thus far. Up until now our approach has relied on two major outcome measures of

motor output – corticospinal excitability using TMS, and muscle activity in the stepping leg. First, we wished to determine if underlying motor regions are in fact, affected by the sight of a graspable object. In these studies, we use TMS to get a ‘snapshot’ of motor output in different visual conditions and the primary measure is an MEP. Future work will explore this in further detail. For example, we would eventually like to include reach-to-grasp kinematics to determine if motor pre-set corresponds to successful grasping characteristics. Second, to measure the stepping response, our present approach has focused on the muscle activity in the ankle dorsiflexors (used to lift the foot to step forward). We believe this offers a sensitive measure of tendency towards a step or not. However, we are in the process of using the embedded force plates to detect postural shifts to reflect the decision to step. This is consistent with the work of Cohen et al, (2011) where the authors measured errors in anticipatory postural adjustments preceding a step, and found that these were inhibition errors during a choice-stepping reaction task in older adults.

Minor Concerns:

***Minor point 1:** Some references seem to be incomplete (line 322, line 342).*

Response: Thank you for catching this oversight. These references have now been included in the revised manuscript. Specifically: Rydalch et al, (2019) and Gibson (1979).

***Minor point 2:** It seems that an important component of this work is to facilitate our understanding of how the brain utilizes contextual information to update which movement would be most appropriate given the surroundings. This is noted in the manuscript, but authors may consider emphasizing it more in the discussion as possible with word restrictions.*

Response: Thank you for your comment. We have now added the following to our revised *Discussion* section:

“An important aim of ongoing work our laboratory is to understand of how the brain utilizes contextual information to update which movement would be most suitable to prevent a fall given the surroundings. Cues such as the availability of a stable handhold or a potential step barrier can guide which response to make should the need arise and may covertly shape predictive brain processes. Notably, the capacity to appropriately use this information may deteriorate with age if mental faculties such as inhibitory interference control or visual-spatial memory are required. Given the relationship between cognitive decline and falls, implementing study designs that emphasize a need for integrating contextual relevance could provide valuable insight into balance deficits in many vulnerable populations.”

Appendix

Stop Signal Task

In the SST, the participant is repeatedly exposed to a 'go' cue and asked to quickly press a button on a keyboard. Occasionally, a stop signal follows the go cue, indicating that the participant should withhold action. The SST is designed to estimate the stopping process by manipulating specific variables in a performance tracking algorithm. A race ensues between two independent mental processes - a go, and a stop process – and this model provides theoretically justified estimates of the latency of stopping¹. Such estimation is necessary given the unobservable latency of the stopping process. Our SST program was custom written in Matlab (Mathworks, MA), adapted from a version used by Aron & Poldrack². This test is completed while participants sit at a desk facing a computer. They will be presented with a go signal (“<” or “>”) and instructed to respond as quickly as possible by pressing the appropriate button on the keyboard (i.e. press “>” if the arrow points right, and “<” if the arrow points left). They will be asked to do this as quickly as possible once the arrow appears, but to refrain from responding if a stop tone is heard. On 25% of the trials, the stop signal follows the go cue at random. The delay between go and stop signals is referred to as the stop-signal delay. The basic idea is that inhibition of the prepotent response is more difficult when the inhibitory stimulus is presented after a longer time interval than a shorter one. When the stop signal is presented close to the go stimulus onset, a response is easier to inhibit however, as the onset of response execution approaches, stopping becomes increasingly difficult. Because the actual latency of the stopping process cannot be directly measured it must be estimated from a stochastic model, and in this way the covert stopping process (SSRT) is estimated. The stop-signal delay is varied to yield a 50% probability of correctly inhibiting a go response after a tone. The delay where participants inhibit their reaction 50% of the time, is used to estimate the SSRT.

References for Appendix:

1. F. Verbruggen, G.D. Logan, Models of response inhibition in the stop-signal and stop-change paradigms, *Neurosci. Biobehav. Rev.* 33 (2009) 647–661.
2. A.R. Aron, R.A. Poldrack, Cortical and subcortical contributions to Stop signal response inhibition: role of the subthalamic nucleus, *J. Neurosci.* 26 (2006) 2424–2433.

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Author(s):	David A E Bolton, Mahmoud Mansour

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