Neural integration in the serial control of reaching and holding still Scott Albert, Alkis Hadjiosif, Jihoon Jang, John W. Krakauer, and Reza Shadmehr

"Posture follows movement like a shadow..." – Sir Charles Sherrington. The nervous system must continuously switch between periods of moving and periods of holding still. For eye movements, separate neural circuits in the brainstem¹ are responsible for these two periods of control: a "hold circuitry" engages the motoneurons based on the commands that the "move circuitry" produced during the preceding saccade. Here, we show that a similar principle links control of movement and posture for the arm: a postural control system produces a field of converging forces that depend on the motor commands that were produced in the preceding reaching movement. Cortical stroke does not alter this dependence, suggesting that the arm postural controller resides not in the cerebral cortex, but in the brainstem or spinal cord.

A total of 158 healthy adults and 5 stroke survivors participated in our studies. To quantify response characteristics of the arm postural controller, we displaced the hand slowly while participants were distracted with a working memory task (Fig. 1A). As the hand was displaced, the postural controller produced restoring forces (Fig. 1B). Did this postural field depend on the move commands that transported the arm during the preceding reach? To answer this question, we asked the participants to reach to a target, but in a velocity-dependent curl force field. Once the reach ended at the target, in most trials we held the hand still using a 2D error clamp, while in other trials we measured the postural field. We found that as the subject adapted and their reach forces changed, so did the field produced by the postural controller: the null point of the postural field shifted so that it no longer aligned with the target of the reach (Fig. 1B). In a separate experiment, we adapted participants to a velocity-dependent force field, but this time repeatedly probed the postural field throughout the adaptation process. We found that the null point of the postural field (Fig. 1C, the zero-crossing where subject forces switched direction) shifted gradually as the subjects adapted. These results demonstrated that the field produced by the postural controller depended on the forces produced during the preceding movement.

How did the time-course of forces during movement affect the postural field? Rather than displacing the hand to measure the postural field, we indirectly inferred its null position from the static forces² that the arm produced as the hand was held still (Fig. 1C). We found that during holding, the arm produced a static force that linearly scaled with the position of the hand with respect to the null point of the postural field (Fig. 1D). We therefore gradually adapted reaching movements to a force field and measured the relationship between moving forces and holding forces. We found a striking relationship: the holding forces at the end of the reach were accurately predicted by the integral of the moving forces that brought the hand to the target (Fig. 2A). In a series of experiments, we found that this coupling of holding force to the preceding moving force persisted across a range of conditions (Fig. 2B): reaches away from (Exp. 1-4,8-10) and towards the body (Exp. 5), at an oblique angle (Exp. 6,7), reaches centered to the left and right of the midline of the body (Exp. 2,3), reaches that lasted approximately 0.5 seconds (Exp. 1-7,10,11) as well as 0.9 seconds (Exp. 8,9), and finally in cases where moving forces switched direction trial-to-trial in multi-target (Exp. 5) and dual adaptation³ (Exp. 4) paradigms. Together, these experiments indicated that the motor commands generated during the move phase were integrated to produce a postural field that specified a null point in space.

Linking movement and holding via mathematical integration is precisely how the oculomotor system is controlled: separate brainstem nuclei control eye movements and gaze holding⁴. David Robinson termed the holding nucleus the "neural integrator" as these neurons receive an efference copy of velocity-related movement commands which they accumulate over time to produce a static position-related output. Is it possible that for control of arm movements, the nervous system also integrates the history of forces to specify the postural field at movement termination? To answer this question, we gradually adapted subjects to a force field that was present only during the 2nd half of the reach (Fig. 3A, unidirectional). As before, we noted that the holding force increased with the integral of the moving forces. Next, we gradually added an opposing force field during the 1st half of the reach (Fig. 3B, bidirectional). In this way, we guided the subjects to produce forces that integrated to zero by the end of their reach. Strikingly, as the integral of the moving forces approached zero, the holding force gradually vanished (Figs. 3B,C). This confirmed that the holding force depended on the entire history of the moving force, consistent with the hypothesis that the postural controller acted as a mathematical integrator of the forces that the limb produced during the preceding movement.

Where in the nervous system does this process of integration take place? To coarsely localize the postural controller, we recruited patients who had survived a cortical stroke. Remarkably, despite the clear presence of stroke-related motor deficits, the integration property of the postural controller remained intact: in both the paretic and non-paretic arms of the patients, the holding forces were tightly coupled to the integral of the preceding moving forces (Fig. 4A,B).

In summary, we found that in both healthy people and in cortical stroke, the postural field during holding depended on the forces that were produced in the preceding reaching movement. This dependence resembled mathematical integration, a principle that is also present in the control of the eyes. Furthermore, we found evidence that despite cortical damage, the dependence of the postural field on the moving forces was conserved. If confirmed, our results imply an anatomical separation of the neural systems for control of arm movement and arm posture, with the postural controller residing in the brainstem or spinal cord.



Figure 1. Adaptation of movement leads to a shift in the null point of a postural field. A. Participants (n=46) reached between two targets while holding the handle of a robotic arm. During the movement, a gradually increasing force field was applied to the hand (FF). The forces produced by the subject after adaptation were measured in error-clamp channel trials (EC). At the end of most reaches a two-dimensional clamp was applied to the hand to hold it in place, preventing any error in the holding process. On some trials, while holding the hand at the target, a memory task was presented where subjects were required to remember numbers presented serially in time. During this distraction, the robot slowly displaced the hand (Postural probe). We hypothesized that the arm would prepare a postural field whose forces were directed towards a null point. **B.** Before adaptation, the postural field exhibited a null point centered at the final hand position (top, color indicates the magnitude of the restoring force, arrows indicate direction of restoring force). After adaptation, the postural field were anoty in the masured moving, holding, and null point probe forces at regular intervals. After the termination of the move forces ("move", approx. 0-0.5 sec) we found that subjects continued to produce a static force while holding ("hold", approx. 0.5-1.6 sec). The robot the nmoved the hand of the subject in the direction of the holding force while subjects were distracted with a memory task. If the holding forces were caused by a displacement from a null point, we hypothesized that these forces would diminish as the null point was approached and then switch directions at the null point (Fig. 1A, Null point hypothesis). Indeed subject behavior exhibited this phenomenon as indicated by the point of zero crossing marked by the "null point" line on the right. **D.** Consistent with a linear spring, we found that the static holding forces linearly encoded the displacement from the null point of the arm.



Figure 2. The holding force at the end of movement is determined by an integral of the moving force. A. Participants (n=15) were adapted and de-adapted gradually to a velocity dependent force field. At the end of each reach, the hand was clamped as in Fig. 1A. By removing error in the holding process, a clear relationship between moving and holding forces was unmasked. The static hold force at the end of movement was tightly coupled to the integral of the moving forces. B. We next probed the coupling between moving and holding across many experiment conditions. In Exp. 1 (n=15) reaches were made away from the body, centered at the midline. In Exp. 2 (n=9) and Exp. 3 (n=8), participants reached to the left and right of midline. In Exp. 4 (n=14) participants were adapted to both a CW and a CCW force field at the same time. In Exp. 5 (n=13), participants reached to two different targets. In Exp. 6 (n=11) and Exp. 7 (n=17), participants reached to a target located at an oblique angle. In Exp. 8 (n=14) and Exp. 9 (n=11) participants were exposed to a position-dependent field (described in Fig. 3). Finally, in Exp. 10 (n=19) participants periodically were exposed to an attention-demanding task (described in Fig. 1). In all cases, it appeared that a simple linear relationship captured the relationship between holding forces and integrals of moving forces.



exposed to a position-dependent force field in two different experiment phases. During the first phase, reaching movements were perturbed by a force field only during the 2nd half of the movement (labeled FF2). After gradually learning this force field, the second phase began. During this phase, an opposing force field (labeled FF1) was generated during the first half of the reach. In this way, subjects gradually learned to compensate for a force field where moving forces would integrate to zero (left-most schematic). **B.** During Phase 1 both the movement integral and the holding forces increased. During Phase 2, as the moving force integral went to zero, holding forces also gradually diminished. **C.** By comparing the holding forces in the unidirectional and bidirectional force fields, it was clear that the neural integrator accumulated moving forces during both the 1st and 2nd halves of the reach.



Figure 4. The neural integrator may reside in a subcortical structure. **A.** To localize the neural integrator we recruited a set of 5 patients that suffered from a cortical stroke. We reasoned that if the process of neural integration remained intact in the paretic limb, this would indicate that the neural integrator may reside in a subcortical region. We found that stroke patients exhibited holding forces in both the paretic and non-paretic limbs, despite mild impairment in adapting to the CW and CCW force fields. **B.** The linear relationship between an integral of moving forces and holding forces remained intact in both the paretic arm). These findings offer preliminary evidence that the neural integrator may be located within a subcortical region of the nervous system.

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