Neural Mechanisms of Limb Position Estimation in the Primate Brain

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Abstract—Understanding the neural mechanisms of limb position estimation is important both for comprehending the neural control of goal directed arm movements and for developing neuroprosthetic systems designed to replace lost limb function. Here we examined the role of area 5 of the posterior parietal cortex in estimating limb position based on visual and somatic (proprioceptive, efference copy) signals. Single unit recordings were obtained as monkeys reached to visual targets presented in a semi-immersive virtual reality environment. On half of the trials animals were required to maintain their limb position at these targets while receiving both visual and non-visual feedback of their arm position, while on the other trials visual feedback was withheld. When examined individually, many area 5 neurons were tuned to the position of the limb in the workspace but very few neurons modulated their firing rates based on the presence/absence of visual feedback. At the population level however decoding of limb position was somewhat more accurate when visual feedback was provided. These findings support a role for area 5 in limb position estimation but also suggest that visual signals regarding limb position are only weakly represented in this area, and only at the population level.

I. INTRODUCTION

Visually-guided reaching movements require the integration of visual and somatic feedback in order to estimate limb position before, during, and after movement. However the mechanisms underlying this integration process, as well as limb position estimation in general, remain poorly understood. In the sensory domain, integrating information across modalities can reduce uncertainty in estimated position. This is achieved by weighting each modality according to its relative reliability, a process referred to as 'optimal cue integration'. Although a large amount of theoretical and psychophysical work exists in support of optimal cue integration, neurophysiological support is relatively lacking. This is due to the fact that testing the predictions of this theory neurophysiologically can be challenging, particularly in the arm movement system. For example, although visual and auditory cues associated with extrinsic objects do on occasion occur in isolation, visual cues about arm position never occur naturally without

concomitant somatic input. This limits the ways in which optimal cue integration can be probed in the arm movement system and also limits the ways in which data obtained from studies of multisensory integration for the arm can be interpreted. As a result of these and other difficulties, studies of the neural mechanisms of multisensory integration for arm movements have not to date explicitly examined whether limb position activity in arm movement related areas is consistent with optimal cue integration.

Although a direct neurophysiological investigation of optimal cue integration for the arm is problematic, it is still possible in this system to assess the role of unimodal and multimodal signals in limb position estimation. This could be accomplished in a number of ways. For example, one could artificially alter the relative reliability of individual unimodal cues and examine the resulting effects on neural responses, as Angelaki and colleagues have done in their studies of self-motion perception in macaque visual cortex [1]. Alternatively, one could simply examine the responses of neurons to two or more cues presented together or in isolation. Additional insights into mechanisms of cue integration could be achieved with this approach by also taking advantage of 'natural' variations in the reliability of different unimodal cues. For example, the relative reliability of somatic and visual signals in estimating arm position has been shown to vary as a function of arm configuration [2-3]. Thus, by varying limb configurations across the workspace while simultaneously varying the number of available sensory signals, one could obtain substantial insight into the role of these signals in limb position estimation.

Which arm movement related brain areas are best suited for probing the neural mechanisms of limb position estimation? Ideally these areas would contain neurons that respond to both visual and somatic signals. In non-human primates several areas have been implicated in the integration of somatic information with visual information of limb position near the body. These areas include the putamen, ventral/dorsal premotor cortex (PMv/d), and the following parietal areas: 5, 7, the medial intraparietal area (MIP) and the ventral intraparietal area (VIP) [4-8]. Any of all of these areas could serve as a target of investigation of the neural correlates of limb position estimation.

Previous studies suggest that area 5, located in the superior parietal lobule (SPL) of the posterior parietal cortex (PPC), would be a particularly good candidate for probing the neural correlates of limb position estimation. For example, in humans, injury to the SPL has been shown to result in

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profound difficulty in maintaining limb position and grip force in the absence of vision, supporting a role for this structure in integrating sensory and motor information for the purposes of estimating limb 'state' [9]. In addition, in non-human primates, the SPL has been shown to receive both visual and somatosensory inputs [10-12] as well as an efference copy of ongoing arm movement commands [13]. This latter finding is supported by anatomical studies indicating direct projections from PMd and motor cortex to area 5 [12].

Neurophysiological studies of non-human primates also suggest a role for area 5 in the integration of somatic and visual limb position cues. In an experimental paradigm where a monkey's unseen arm was passively varied between positions that were either congruent or incongruent with the position of a visible, fake monkey arm, Graziano and colleagues (2000) found that area 5 neurons encoded the position of the unseen arm as well as the position of the seen, fake arm. Variations in discharge due to manipulations of the unseen or 'felt' arm were attributed to somatic signals, while variations due to the fake 'seen' arm were interpreted as being related to visual information about limb position. These findings were interpreted as evidence that area 5 is involved in integrating visual and somatic signals about limb position. However, in this study animals were not required to make a perceptual judgment nor were they required to actively control the position of their limbs. Thus, it is unclear the extent to which the animals perceived the fake arm as being part of their own bodies.

The integration of visual and somatic limb position signals in area 5 has been studied more recently in a task that required animals to maintain their limb position while actuating pushbuttons on a vertically oriented target array (C. A. Buneo & R. A. Andersen, unpublished observations). These experiments showed that most area 5 neurons encoded the position of the arm in eye-centered rather than body-centered coordinates, even in the absence of visual signals about the arm. This suggests that somatic and visual information about arm position are encoded in the same eye-centered reference frame in area 5, which could arise as the result of somatic signals being transformed from body to eye-centered coordinates. In addition, as in the study by Graziano and colleagues (2000), a subset of neurons was modulated by visual signals about the arm. However, the relatively small percentage of neurons (~15-20%) is not what one would expect of an area that plays a critical role in estimating limb position based on both visual and somatic signals. This could be a consequence of the experimental paradigm, where the combination of tactile, proprioceptive and force feedback experienced by the animals during the button presses likely provided a very reliable estimate of limb position, reducing the importance of visually-based limb position signals. As a result we sought to examine the integration of visual and somatic signals in area 5 under conditions where visual information should be more critical to task performance, i.e.

during the maintenance of static limb positions in free (3D) space.

II. METHODS

A. Experimental Methods

Two head-fixed animals have been trained to make arm movements within a computer-generated, 3D virtual environment, similar to the one employed by Schwartz and colleagues [14]. This paradigm is ideal for studying the responses of neurons in the presence and absence of visual input, as it allows complete control over the degree and timing of visual feedback. A schematic of the experimental apparatus is shown in Fig. 1a. In brief, arm movements were monitored using an active LED based motion tracking system (Visualeyze VZ3000, Phoenix Technologies Inc., sampling rate: 250 Hz, spatial resolution: 0.015mm at 1.2m distance). Vision of the animal's arm was blocked by a mirror, but the position of the endpoint of the arm (the wrist) was viewed by the animal as a spherical cursor displayed on a 3D monitor (Dimension Technologies Inc.) and projected onto the mirror. Eye movements were monitored using a remote optical eye tracking system (ASL Inc., sampling rate: 120 Hz, spatial resolution: 0.25 degrees of visual angle).
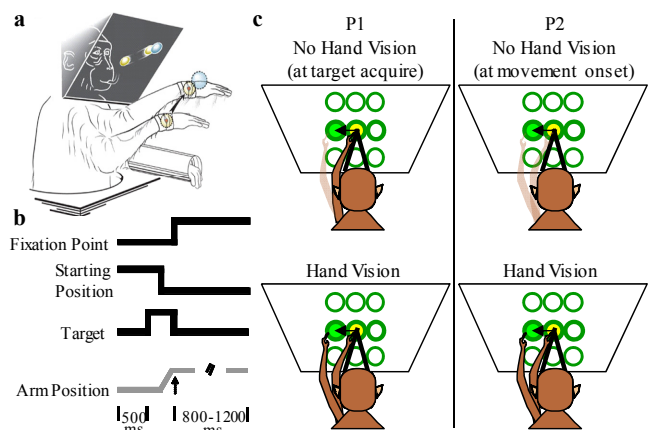

Fig. 1. Behavioral methods. (a) Schematic of virtual reality setup. Adapted from Taylor et al. (2003). Courtesy of S. Helms-Tillery. (b) Sequence of events on a single trial for Paradigms 1 and 2 (P1 & P2). Arrow indicates acquire time of target. (c) Schematic of behavioral paradigms P1 and P2. Animal and target display are viewed from behind; targets (circles) are located in a vertical plane surrounding the central starting and fixation position.

Two basic experimental paradigms were used. For both paradigms, at the start of each trial, a green target sphere was presented in the center of the virtual workspace. Once this position was acquired and maintained for 500 msec, a second green target sphere was presented at one of 8 positions in a vertical plane. The location of these potential targets with respect to the animal is shown in Fig. 1c. The presentation of the second target sphere instructed the animal where to place its arm and also served as a 'go' signal, cueing the animal to move its arm to the target. In Paradigm 1 (P1), the spherical

cursor representing the endpoint of the arm was visible at the beginning of each trial as well as during the movement toward the second target. Once the second target position was acquired, visual input of the endpoint of the arm continued to be allowed on visual trials but was disallowed on somatic trials by blanking the arm cursor. For both types of trials, the animal was required to maintain its arm position during a static holding period of between 800 and 1200 msec, while simultaneously maintaining visual fixation at the center of the target display. This sequence of events was repeated until 5 trials were performed to each target. For Paradigm 2 (P2), the sequence of behavioral events was the same except that on somatic trials the arm cursor was blanked at movement onset, rather than at the time of acquisition of the second target.

Thus far, neurophysiological recordings have been made in dorsal area 5 of the SPL. Single cell recordings (N = 333) have been obtained from one of the animals (Macaca mulatta) using standard neurophysiological techniques. Activity was recorded extracellularly with varnish-coated tungsten microelectrodes (~1-2MΩ impedance at 1 kHz). Single action potentials (spikes) were isolated from the amplified and filtered (600-6000 Hz) signal via a time-amplitude window discriminator (Plexon Inc.). Spike times were sampled at 2.5 kHz.

B. Data Analysis

At the single cell level the effects of limb position and the visual conditions (vision of the hand ('vision') vs. no hand vision ('no-vision')) on mean firing rate during the static holding period were assessed using a 2-factor analysis of variance (ANOVA, $p < 0.05$). At the population level these effects were assessed using a Bayesian decoding approach, similar to that described in Scherberger et al. (2005) [15]. For this analysis, cells were considered to be simultaneously recorded. Activity during the static holding period was used as input to a decoding algorithm that was used to predict the location of the limb on a given trial. A value of 1 was assigned to correctly predicted trials and a value of 0 to the incorrectly predicted ones. The means of the sequences of correctly and incorrectly classified trials were represented graphically as confusion matrices (see Fig. 4).

III. RESULTS

A. Behavior

In order to properly investigate the influence of visual and somatic signals on limb position activity in this experiment it was critical that animals exhibited identical endpoint positions on vision and no-vision trials for each target location. That is, any difference on the two trial types must reflect the manner in which vision and somatic information are processed in the PPC and cannot be due to the fact that the animal held its arm at slightly different positions in space on the two trial types, a distinct possibility in this type of experiment. To guard against this possibility we recorded the

animal's limb position during the time when the animal was holding its arm at each target and compared the distribution of endpoints for the two trial types. For P1, no consistent differences in the two distributions of endpoints were observed indicating that the animals did indeed exhibit the same behavior on vision and no-vision trials. For P2, differences in movement endpoints were often observed but were not generally consistent from session to session.

B. Neurophysiology

Despite these behavioral differences, neural responses were relatively consistent between paradigms, in terms of sensitivity to position and visual feedback condition. Figure 2 shows neurophysiological data from a single area 5 neuron in P1. Each panel corresponds to a single location in the vertical plane. Peristimulus time histograms of the average firing rate during vision (red) and no-vision trials (green) are shown. Data are aligned at the time of acquisition of the target.
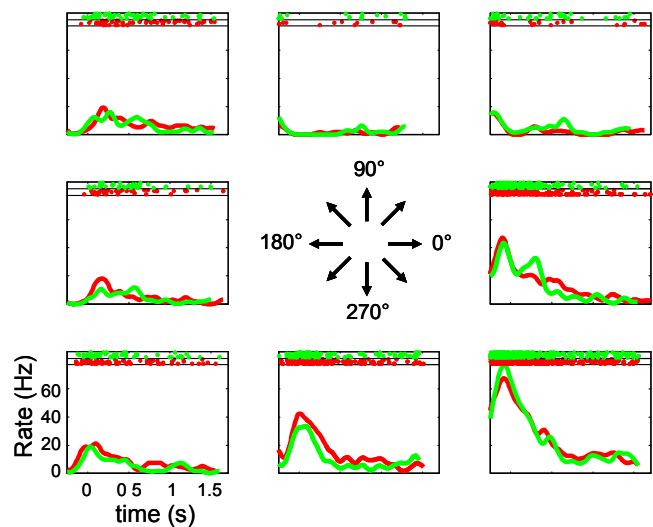

Fig. 2. Activity of an area 5 neuron on hand vision trials (red) and no hand vision trials (green). Data are aligned to target acquire. The arrows in the center point to 8 different movement directions associated with each pannel.

There are several points to be made regarding this figure. First, this cell exhibited tuned perimovement activity (as evidenced by the burst occurring slightly before time 0) as well as tuned static positional discharge. For both types of visual feedback conditions, discharge was greatest when the animal held its hand at the target located in the lower left position of the display (225°). Second, the activity of this neuron was very similar on vision and no-vision trials. That is, even after the visual stimulus corresponding to the endpoint position was extinguished on no-vision trials (T=0.4 s), the neuron continued to fire in roughly the same manner as on visual trials. An ANOVA on the mean firing rate during the static holding period indicated a main effect of position but no effect of the visual conditions and no position/visual conditions interaction. Thus, this neuron either encoded static limb position using only somatically derived information, or if it did receive visual input it weighted this

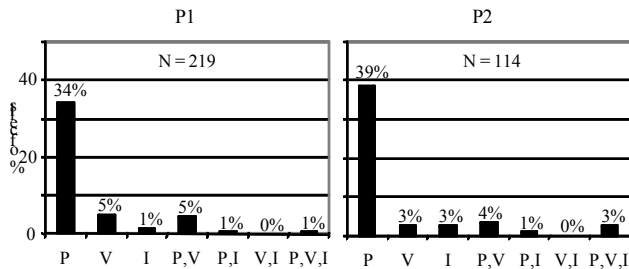information minimally in the context of this task.

Fig. 3. Results of ANOVA for the population of cells studied in P1 and P2. P: Main effect of position. V: Main effect of visual feedback conditions. I: Interaction between position and visual feedback conditions.

The similarity between paradigms in terms of sensitivity to position and visual feedback condition is summarized in Fig. 3. For both paradigms, neurons with positional activity were quite common (42% of the population for P1; 50% for P2). In contrast relatively few cells showed effects of visual feedback condition (13% for P1; 14% for P2).
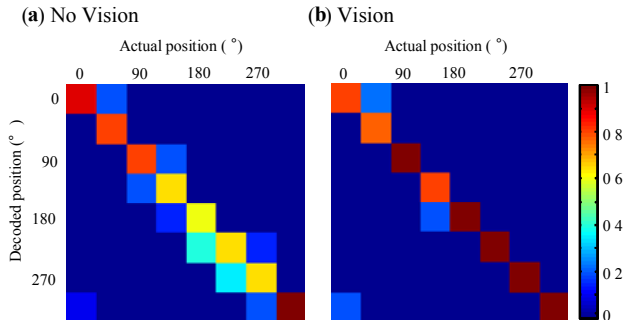

Fig. 4. Results of Bayesian population decoding analysis in P1. Color indicates the probability of decoded position given the actual position. The accuracy of position decoding for many positions increased in the presence of vision.

We have recently begun using decoding techniques to probe the roles of visual and somatic signals in representing limb position in this area. Figure 4 shows the results of some of these analyses using neurons that demonstrated effects of position but no effect of the visual feedback conditions according to the ANOVA. Despite the fact that the ANOVAs for this population did not generally show an effect of the visual feedback conditions, decode performance was noticeably different depending on the presence or absence of visual feedback. That is, performance was reasonably accurate in the absence of hand vision but improved when vision of the hand was simultaneously available. Similar results were obtained when cells that were tuned to both position and the visual feedback conditions were used. These results suggest that the ANOVA lacks the sensitivity required to fully assess the effects of vision in this task. Moreover, the results suggest that visual signals may in fact play a role in representing limb position in this area.

IV. CONCLUSIONS

Previous results have suggested that visual information

regarding arm position is not strongly represented in area 5. However, these results were obtained in tasks where animals were either not reaching to objects in their environment or under conditions where the animals were receiving strong haptic input on visual trials, which could have influenced the weighting of vision. The present results extended these observations to conditions where vision would be expected to have the greatest influence, i.e. under conditions where the arm is held statically in free space. Under these conditions relatively few individual area 5 neurons appeared to integrate visual information about limb position with somatically-derived signals. However, a decoding analysis showed that vision does appear to play a role in representing limb position in this area at the population level. The relatively modest nature of these effects suggests that the primary site of integration of visual and somatic limb position information is likely downstream of area 5.

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