Summary

Integration of somatosensory afferent signals for control of muscle activity during voluntary arm movements

SOKENDAI (The Graduate University for Advanced Studies)
School of Life Science
Department of Physiological Sciences
Nishihara, Yoko

Introduction

Somatosensory information is essential for coordinated limb movements. Peripheral sensory receptors continuously transmit somatosensory information to the central nervous system, which is critical for us to perform the precise limb control, and their blockade impairs the fine motor control.

Somatosensory information, including proprioceptive and tactile information from muscles, joints, and skin, is carried from the peripheral sensory receptors to the dorsal root ganglia (DRG) located adjacent to the spinal cord. The central branches either ascend to the supraspinal centers or make reflex loops in the spinal cord towards targeting motoneurons. The latter pathway forms spinal reflex circuits for generating stereotypical movements by rapid feedback corrections. However, how peripheral sensory feedback is involved in the modulation of muscle activity during voluntary movements is unclear.

To understand the contribution of peripheral sensory feedback to voluntary movements, I simultaneously recorded the activity of a population of peripheral afferents and corresponding forelimb muscles in two monkeys during a voluntary reach-and-pull task. The muscle activities were decoded from the population activity of DRG neurons. The decoding model was also examined to reveal how the population activity of DRG neurons was integrated to modulate muscle activity.

Methods

Behavioral task and physiological recordings

Two macaque monkeys (Macaca fuscata), one female (Monkey C, 5.4kg) and one male (Monkey T, 5.9kg), were trained to perform a reach-and-pull task with their right hands. During the task, single-unit activities were recorded from a population of DRG neurons at the lower cervical segments (Monkey C: C6, 13 units; Monkey T: C7-C8, 17 units) by using multi-electrode arrays (sampling rate: 40 kHz). Population activities were filtered by a multi-channel amplifier (150 kHz high-pass and 8 kHz low-pass analog filters) with a gain of x20000. At the same time, electromyogram (EMG) from forelimb muscles (Monkey C, 10 muscles; Monkey T: 12 muscles) was also recorded (sampling rate: Monkey C: 1 kHz, Monkey T: 2 kHz). Activities of EMG were also filtered by an additional amplifier (1.5 high-pass and 3 kHz low-pass filter).

Decoding muscle activity from DRG neuron activity

A sparse linear regression algorithm (SLiR) was applied to decode the activity of individual muscles from the DRG neuron activity, as follows:

$$y(t) = \sum_{k,l} w_{k,l} \times x_k\left(t + l\delta\right) + b$$

where $y(t)$ is a vector of the EMG signal from a single muscle at time index t. $x_k(t+l\delta)$ is an input vector of DRG units k (13 or 17 units) at time index t and time-lag $l\delta$ (δ = 5 ms). $w_{k,l}$ is a vector of weight coefficients on DRG units k at time-lag $l\delta$, and b is a vector of the bias term associated with y. The SLiR can automatically extract appropriate inputs and discard unessential signals to achieve a good generalization performance. So this algorithm can avoid overfitting problem compared to regularized linear regression models. SLiR has been used for studying population coding of DRG neuron activity.

Decoding with different time lags

I decoded activity of each muscle from activity of all DRG neurons with a time lag between them (lags ranged from -500 ms to 500 ms, with a step width of 50 ms or 10 ms). With the positive lags (lags > 0), the DRG activity was used to predict muscle activity that occurred earlier. High decoding performance with a positive lag implies that information in the muscle activity is carried on to the later DRG activity. This would be expected that somatosensory information reaches to DRG after actual movements. With the negative lags (lags < 0), the DRG activity was used to predict muscle activity that occurred later. High decoding performance with a negative lag implied that information in the DRG activity is carried on to the later muscle activity. This would suggest that somatosensory afferent information is involved in the generation of upcoming muscle activity. In this thesis, the zero lag was treated as the negative values because the DRG neuron activity with the zero lag should have already carried the somatosensory information.

For the model estimation and evaluation, a recording session (10 min) was divided into 24 blocks (25 s each). Among 24 blocks, 21 blocks were randomly selected as the training blocks to estimate the decoding model. The remaining three blocks were used as the testing blocks to cross-validate the decoding performance (both correlation coefficients and root mean square error were used). The combinations of testing and training blocks were changed 8 times so that each block was chosen once as the testing block. Eight-fold cross-validation was performed in all the analysis.

The DRG neuron signals were transformed from discrete (spike timing) to continuous (instantaneous firing rate) signals with linear function kernels. The EMG signals were filtered

(bandpass: 30-60 Hz, butter-worth, n = 2), rectified and smoothed (moving average with a window size of 11). Then both DRG and EMG signals were down-sampled to 200 Hz.

For each muscle, a total of 37 decoding models were estimated, one for each time lag. Each decoding model was obtained from the following procedure: (1) The preprocessed EMG signals were decoded from the preprocessed DRG signals by using the SLiR, and (2) the correlation coefficient (R) and normalized root mean square error (nRMSE) between the actual and decoded EMG signals were calculated to evaluate the decoding performance.

Determination of the informative lags

I identified the lags during which the decoding performance exceeded the chance level. To achieve this, I shuffled the combination of DRG neuron signals and EMG signals in the training blocks and obtained a shuffled model. In the shuffled model, the causal relationship between the DRG and muscle activity would be removed, and thus the decoding performance of the shuffling model could be regarded as the chance level. This shuffling procedure was repeated 50 times for all lags.

For each lag of a muscle, the decoding performance (i.e. R and nRMSE) of the original unshuffled case was compared to its corresponding chance level (unpaired t-test, $\alpha = 0.05$, Bonferroni correction). A lag with decoding performance significantly higher than the chance level was defined as an "*informative lag*".

Contribution of DRG unit to single muscle

For each lag of a muscle, I compared the weight coefficients of the decoding model obtained from the original unshuffled case to those obtained from the shuffled case (unpaired t-test, $\alpha = 0.05$, Bonferroni correction). If a weight coefficient was significantly different from the shuffled counterpart, the DRG unit associated with the weight coefficient was defined this as an "*informative unit*".

I then counted the number of informative units for each muscle in each lag. I also counted the number of muscles that each DRG unit significantly contributed to. This analysis was only performed for the decoding models with the informative lags.

Results

Decoded muscle activity

The activity of 10 muscles was decoded from 13 DRG units in Monkey C. The activity of 12 muscles were decoded from 17 DRG units in Monkey T. In the case of positive lags, the muscle activities of each muscle were decoded accurately for the whole time course (e.g. EDC, lag = 30 ms, R: mean ± std, 0.61 ± 0.12, nRMSE: 0.67 ± 0.04 in Monkey C; R: 0.69 ± 0.11, nRMSE: 0.62 ± 0.05 in Monkey T). This suggested that the DRG neurons encoded the muscle activity, as expected. In the case of negative lags, only the later phase during the movement period could be decoded, so the decoding performance were slightly lower than in the positive lags (e.g. EDC, lag = -20 ms, R: 0.40 ± 0.16, nRMSE: 0.77 ± 0.03 in Monkey C; R: 0.48 ± 0.20, nRMSE: 0.70 ± 0.07 in Monkey T). This result suggested that the peripheral afferent feedback signals in DRG neurons contributed to the control of muscle activity, especially for the later phase of the movement.

The chance level of decoding performance

The nRMSE was applied to evaluate the decoding performance instead of R. The chance level of R values changed across time lags and oscillated between the negative and positive values while the chance level of nRMSE values showed no significant changes across the time lags. Because the calculation of R values does not consider the difference but only measures the similarity between the patterns of two signals, so R value could show high values even the amplitudes of two signals are significantly different. Since nRMSE is a direct measure of the difference in amplitudes between two signals, nRMSE is considered to be a more appropriate measure of the decoding performance than R, and hereafter I used nRMSE as the indicator of decoding performance indicator in the following analyses.

Determination of the informative lags

I identified the informative lags during which the decoding performance exceeded the corresponding chance level. The informative lag of EDC was ranged from -60 ms to +350ms in Monkey C and from -100 ms to 500 ms in Monkey T, respectively. In all the recorded muscles from the two monkeys, the informative lags included both the positive and negative lag ranges. The informative onset for all muscles was ranged from -30 ms to -350 ms in two monkeys, which indicated that DRG activity which occurred slightly earlier than muscle activity contained the information about the muscle activity.

Contribution of individual DRG activity to muscle activity

Next, I investigated the decoding model itself, because, in a particular decoding model, the weight coefficient value represents the contribution of individual DRG activity to the activity of the target muscle.

(1) Contribution of multiple DRG units to a single muscle

First, I examined the weight coefficients of the decoding model for each informative lags to understand the dynamics of contribution of DRG unit activity to the target muscle activity. For each decoding model, multiple DRG units were involved in the decoding of muscle activity. In a particular model, the weight coefficient value was different among individual DRG units. In each DRG unit, the weight coefficient value dynamically changed across time lags. These results indicated that the contribution of individual DRG units would contribute to the decoding of muscle activity with a variety of temporal profiles.

In multiple DRG units of a particular decoding model, weight coefficient values showed a significant difference from the weight coefficient values of the shuffled models. For example, in EDC of Monkey T, the number of informative units was 8 in a lag (-100 ms). These results indicated that the somatosensory information related to the target muscle was decoded by activity of multiple DRG units. In another lag (-20 ms), the number of informative units was 7. Although these numbers of informative units were close to each other, the combination of the DRG units was partially different.

Thus, these results demonstrated that the number of DRG units that have the somatosensory information related to the muscle activity changed across time lags and that contribution of the individual DRG unit to the decoding of muscle activity also varied across time lags in both monkeys.

(2) Contribution of a single DRG unit to multiple muscles

Second, I compared the weight coefficients across the decoding model for individual muscles to understand how activity from a single DRG unit contributed to the activity of multiple muscles. The examination was done for each unit. For example, the particular DRG unit (unit no.2 in Monkey T) was involved in the 8 muscles (lag = -100 ms). In another lag (lag = -20ms), the same DRG unit was involved in the 9 muscles. The combination of muscles was partially different between these lags. The number of muscles for which the DRG unit has significant information changed across the time lag, which indicated that a particular DRG unit carried the somatosensory information related to multiple muscles. The number of muscles for which the DRG units had significant information also varied across lags.

Thus, these results demonstrated that a particular DRG unit had information for multiple muscles. However, the number of contributing muscles changed across time lags and that contribution of the individual DRG units to the decoding of the muscle activity also varied across time lags in both monkeys.

Discussion

The purpose of the thesis is to examine the integration of somatosensory information to muscle activity during voluntary movements by using a decoding approach. The results, for the first time, demonstrated that the activity of multiple forelimb muscles could be decoded from the peripheral afferent activity of DRG neurons in lower cervical segments, during voluntary movements. Particularly, I found that some muscle activity could be decoded from DRG activity occurred slightly earlier, which supported the hypothesis that somatosensory afferent signals play an important role in the control of ongoing voluntary movements. The examination of the decoding models further revealed the dynamics of integration of peripheral afferent signals in the spinal cord. This sensory integration could subserve a mechanism to modulate target muscle activity in convergent and divergent manners, and provide fine-tuned and flexible online corrections for the coordinated and smooth movements of the forelimbs.