Muscle synergy for coordinating redundant motor system

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"How does the brain rapidly and flexibly control our body?"

This is the underlying question of my study. Biological system essentially contains an immense number of control variables. Our arm, for example, controls 7 degrees-of-freedom despite the hand position in 3-dimensional workspace, indicating the redundancy in the kinematic and kinetic spaces. Even if the joint torques were determined, more relevant muscles contribute to the joint torques than the number of the controlled joints. Accordingly, the central nervous system (CNS) has to select one appropriate solution within an infinite number of solutions to execute movements. Bernstein (1967) called this ill-posed problem a degree-of-freedom problem, which has been the fundamental issue in all motor control studies (Bernstein, 1967). To simplify the redundancy at a muscle activation level, the concept of a muscle synergy was proposed (Tresch et al., 1999). A muscle synergy modularly organizes multiple muscles as a same group with different synaptic weights and the combination of muscle synergy activations enables the CNS to generate a wide range of muscle activation patterns. In this concept, a muscle synergy contributes to the reduction of the control variables because the CNS modulates low-dimensional activation patterns of muscle synergies rather than individual muscles. The robustness of muscle synergies was observed in variety of movements (Torres-Oviedo and Ting, 2007; Chvatal and Ting, 2013; Hug et al., 2010). In addition, some physiological findings provided evidence about a muscle synergy in the spinal cord (Saltiel et al., 2001; Hart and Giszter, 2010) or brainstem

(Roh et al., 2011). However, whether a muscle synergy actually exists in the neural circuitry is still controversial (Bizzi and Cheung, 2013). To break through the underlying and crucial issue, it is important to examine the relationship between a conjectural muscle synergy and actually generated output like an endpoint force and, furthermore, to clarify the functional roles of a muscle synergy, which is indispensable in the neural circuit. The critical problem that researchers confront is that the candidate is invisible: a muscle synergy would be encoded within the neural circuit, which can't directly be measured particularly in human, even if a muscle synergy actually exists. To achieve my purpose in that significant issue, I unraveled the mechanisms of a muscle synergy with the combination of the experimental and the model-based approaches. This thesis was composed of 5 experimental and 2 model-based studies as following.

In the experimental part, I first investigated whether the modular control of a single bi-articular muscle, rectus femoris (RF), to determine knee and hip joint torques was fixed or flexible (***Study 1***; Hagio et al., 2012, *Journal of Biomechanics*). As electrically stimulating various sites of RF, the contribution to each joint torque was relatively larger in the close joint. This result suggested that the CNS flexibly modulates knee and hip joint torques using the anatomical region-specificity of RF. In ***Studies 2*** and ***3***, I examined whether the CNS actually produces forces through the neural system of muscle synergies by quantifying the relationship between the activation of muscle synergies and the resultant motor output. As a result, I clarified the correlation between the estimated lower-limb muscle synergies and the resultant endpoint force fluctuations during isometric force generating task around an ankle (***Study 2***; Hagio and Kouzaki, 2015, *Experimental Brain Research*) and then quantified the mechanical contribution of muscle synergies in the 3-dimensional endpoint force space based on the correlation analysis (***Study 3***; Hagio and Kouzaki, 2015, *Frontiers in Bioengineering and Biotechnology*). Thus, the neural system of muscle synergies would be activated to generate endpoint force. In ***Study 4***, I focused on the control mechanism of muscle synergies depending on the force-generating capability of individual muscles. The extraction of muscle synergies during isometric force generating tasks with different knee and hip joint angles demonstrated that similar muscle synergies were recruited in a wide range of joint conditions (Hagio and Kouzaki, 2014, *Journal of Neurophysiology*). In addition, the result indicated that the CNS flexibly modulated the activation of individual muscle synergies with merging or fractionation to properly generate the desired endpoint force depending on the force-generating capability of muscles. Nextly, I extended the workspace to the dynamical space and clarified the modulation of muscle synergies to translate the movement requiring different kinematics, i.e., a gait transition between walking and running (***Study 5***; Hagio et al., 2015, *Frontiers in Human Neuroscience*). The results suggested that a spontaneous gait transition was performed by gradually changing the activation timing of specific muscle synergies, which was composed of plantar flexor muscles, based on afferent information as increasing or decreasing the gait speed whereas the CNS could instantly change the gait patterns by quickly altering the timing of descending neural input to the muscle synergies.

In the computational part, I first revealed the functional roles of muscle synergies during motor learning by comparing the learning performance, such as learning speed and errors, between in the presence and absence of muscle synergies using a descending neural network model (***Study 6***). The neural network model was composed of three intermediate layers, which assumed neurons in primary motor cortex (M1), muscle synergies as spinal interneurons and motoneuron pools controlling individual upperlimb muscles. The isometric torque generating tasks with elbow and shoulder joints were simulated. Each layer was connected with synaptic weights. The weights from input as the target torque to M1 neurons and from muscle synergies to muscles were updated to minimize the error between the desired input torque and output torque using back-propagation algorithm (Rumelhart et al., 1986). As a result, adaptation speed to produce multi-directional isometric forces in a novel environment was increased in the model with muscle synergies as compared to the model without muscle synergies. The simulation further demonstrated that a muscle synergy contributed to the reduction of the essential bias in the musculoskeletal system and then coordinated the neural system so that the CNS can quickly adapt to a novel environment. In ***Study*** *7*, I simulated the process of the formation of muscle synergies using the above neural network model and unraveled that muscle synergies were constructed depending on the frequently used motor output in the optimization framework. According to the results, I proposed a learning algorithm to construct muscle synergies in the nervous system based on self-organization. Using the self-organizing learning algorithm (Kohonen, 2001), the synaptic weights from 2000 neurons on a topological plane to individual motoneuron pools was updated so that the experimentally recorded muscle activation datasets were represented in a population of neurons. As a result, the patterns of synaptic weight were constrained in approximately 4 domains of neurons. These results suggested that a population of spinal interneurons having the similar synaptic weights to individual motoneuron pools macroscopically represents the structure of a muscle synergy.

The interactive studies by combining the experimental and model-based approaches made it possible to clarify the underlying mechanisms of muscle synergies in the neural circuitry. A muscle synergy is necessary as a memory in the biological system not only to simplify the redundancy at muscle activation level but also to properly coordinate the nervous system depending on the individual motor demand. Therefore, the CNS rapidly and flexibly controls our body using the nervous system of a muscle synergy that structure will be ambiguously represented in the neural circuitry.