博士論文

The Switching Mechanism of Muscle Synergies for Lower Limb Control

(下肢制御における筋シナジーの切替機序)

鈴　木　崇　人

Acknowledgements

Dr. Jun Ishibashi raised my awareness as a sole proprietor, and Prof. Tetsuya Amino watched the progress of my early work as a historian, and my supervisor Prof. Senshi Fukashiro has helped my career as a scientist.

Dr. Shinsuke Yoshioka taught me biomechanics. Dr. Dai Yanagihara and Dr. Kazutoshi Kudo imparted basic knowledge about the muscle synergy and uncontrolled manifold hypotheses to me, respectively. Prof. Kimitaka Nakazawa framed my thoughts about the size principle.

Prof. Shu Takagi gave me critical advice. Dr. Junichi Ushiyama, who was introduced by Dr. Kentaro Chino, and Dr. Ryuta Kinugasa told me research methods. I could focus on my work, with the support of Dr. Yuki Inaba, Mr. Yuta Kawamoto, Dr. Kohei Shioda, Dr. Rintaro Ogane, Mr. Shimpei Kubo, Obara Shiraume Scholarship Foundation, RIKEN, and Japan Society for the Promotion of Science.

I say a few words in a scientific manner, which is about selecting uncontradicted evidence; thank you.

Takahito Suzuki

Contents

Chapter I

General Introduction

A history of the muscle-synergy concept

Since ancient times, humans have been interested in the mechanics of human body. The Edwin Smith Papyrus provides evidence that ancient Egyptians investigated human anatomy at least as early as the 17th century B.C. (Breasted 1930a, 1930b). In the second century A.D., Galen reported human anatomy in detail. For example, he separated 14 muscles around the ankle (Goss 1963). These ancient anatomists wondered why one joint had multiple muscles that had a similar function, and how these muscles were controlled.

Galen grouped muscles and termed them agonists and antagonists (Goss 1968). In the 17th century, Descartes proceeded with this idea, and proposed that the agonist and antagonist were connected by nerves and were alternately activated (Descartes 1972). In such a manner, ancient to early-modern scholars had conceived some kind of muscle grouping based on function as one of the ways in which muscles around a certain joint were controlled.

From the late 17th century, the research for muscle activation mechanics rapidly developed (Cobb 2002). Swammerdam discovered that nerve irritation, in which electrical stimulation might have been induced by a brass hook and silver wire (Cobb 2002), leads to contraction of a single muscle in the frog (Swammerdam 1758). In 1791, Galvani observed that electrical nerve stimulation induced contraction of multiple muscles in the frog limb (Galvani 1791). In 1870, Fritsch and Hitzig confirmed functional localization of the motor cortex of the dog by electrical stimulation (Fritsch and Hitzig 1870). Because electrical stimulation to the nerve or cortex induced simultaneous or cooperative activity of muscles, these observers believed in the integrative control of multiple muscles. Consequently, Sherrington used the term

‘synergy’ to describe cooperative activity of muscles, although what was “cooperative” was somewhat ambiguous (Sherrington 1906). In the middle part of the 20th century, Bernstein defined the ancient question regarding the control of multiple muscles as the ‘degrees of freedom problem’ (Bernstein 1967).

Evidence for the existence of muscle synergies

Even assuming the integrative control of multiple muscles, it was difficult to identify the physiological systems that function as muscle synergies. One of the possible sites was the motor cortex (Fritsch and Hitzig 1870). Cortical interneurons and corticospinal and corticomotoneuronal cells could represent muscle synergies (Huntley and Jones 1991). In 1991, Bizzi and colleagues observed that microstimulation of a site in the frog lumbar spinal cord elicited a leg force pattern that was related to several muscles, and simultaneous stimulation of two spinal sites summed two corresponding sets of leg forces (Bizzi et al. 1991). Since 1991, many studies have confirmed the ability of spinal interneurons to simultaneously control multiple muscles in various animals, such as the frog (Hart and Giszter 2010; Mussa-Ivaldi et al. 1994; Roh et al. 2011) and monkey (Takei and Seki 2010). Because spinal interneurons are close to motoneurons, they likely compose a large part of muscle synergies.

Similar to the difficulties experienced clarifying the physiological entity of muscle synergies, it has not been easy to investigate the way muscle synergies are recruited during voluntary movements (Lee 1984). Although correlation between the electromyographic activities of several muscles was observed during a single-joint movement (Bouisset et al. 1977; Buchanan et al. 1986), a mathematical tool that can decompose the mixed electromyographic activity to the recruitment of each muscle synergy was hard to find. In 1999, Tresch and colleagues applied a non-negative least-squares algorithm, which is a computational decomposition technique, to the electromyographic activity of frog limb muscles (Tresch et al.

1999). After this study, computational decomposition techniques for electromyographic activities spread widely among researchers in the field of motor control, and many studies have reported the existence of muscle synergies during a variety of voluntary movements (Cappellini et al. 2006; d'Avella et al. 2003; Roh et al. 2011; Torres-Oviedo et al. 2006).

Challenge to the dependence of human motor control on muscle synergies

The stimulation and behavioral approaches have provided enormous physiological and behavioral evidence of muscle synergies. Nevertheless, the muscle synergy hypothesis has been difficult to strictly prove or falsify (Kutch and Valero-Cuevas 2012; Tresch and Jarc 2009). Doubt has been cast on whether the stimulation approach can elicit the complete repertoire of muscle activation patterns (Kutch and Valero-Cuevas 2012). Even though interneurons are available for the synchronous control of multiple muscles, the specific control of single muscles might be learned and used by the motor cortex (Moritz et al. 2008). Of course, the behavioral approach can examine all practical muscle activation patterns, but it is affected by task constraints that reduce feasible activation patterns, independent of neural control (Buchanan et al. 1986; Kutch and Valero-Cuevas 2012; Lee 1984; Tresch and Jarc 2009). For example, previous studies reported that muscle activities during walking were grouped in a synergy-like manner (Cappellini et al. 2006; Clark et al. 2010; Dominici et al. 2011), but such a grouped muscle activity was roughly predicted by computer simulation that developed around the end of the 20th century (Anderson and Pandy 2001), based on an objective function (Flash and Hogan 1985; MacConaill 1966) unrelated to muscle synergies. Such reduced activation patterns could be misinterpreted as muscle synergies, which are neural constraints. Therefore, the study to prove the muscle synergy hypothesis should distinguish muscle synergies from non-neural muscle activation patterns constrained by a task.

In the 21st century, studies on the variability of the exerted force or muscle activation

have provided evidence against the dependence on muscle synergies during human motor control (Kutch et al. 2008; Tresch and Jarc 2009; Valero-Cuevas et al. 2009). Valero-Cuevas and colleagues applied the uncontrolled manifold approach (Schöner 1995), which has been used to reveal large, task-irrelevant variability of joint kinematics (Scholz and Schöner 1999) and kinetics (Scholz et al. 2002), to muscle activation, and reported that the variability of index finger muscle activities that affected the fingertip force was smaller than their task-irrelevant variability (Valero-Cuevas et al. 2009). One interpretation (Tresch and Jarc 2009) is that this small variability suggests that each muscle was independently controlled and activity that did not affect the task (i.e., the fingertip force) was uncontrolled. This interpretation emphasizes the independent control of muscle activities and somewhat contradicts the hypothesis that muscle activities are simultaneously controlled by muscle synergies (Tresch et al. 1999).

Further evidence is necessary to verify the dependence of human motor control on muscle synergies, and this evidence must be obtained in an experiment that clarifies the mechanical constraints and the variability of muscle activities in a given task.

Thesis Contents

In the thesis, a muscle synergy is defined as a synchronous synergy, i.e., one in which all muscles are activated with no temporal delay (Tresch and Jarc 2009). The purpose of the thesis is to confirm the dependence of lower limb control on muscle synergies and propose the muscle synergy recruitment strategy. For these purposes, the research is presented in four chapters: II–V. Because knee extensor activation at the fully extended position can induce a change in plantar flexor activity at the constant mechanical constraint on plantar flexor muscles, plantar flexor activity during isometric plantar flexion with or without isometric knee extension is analyzed by two-piece linear regression (Chapter II), non-negative matrix factorization (Chapters II, III, and IV), uncontrolled manifold approach (Chapter III), and interpolated twitch technique

(Chapter IV).

The aim of the study reported in Chapter II was to reveal the dependence of plantar flexor muscles on muscle synergies and the difference in this dependence between low and high plantar flexion torques. The mechanical constraint that reduces the feasible muscle activity patterns was carefully controlled, and the results presented in Chapter II showed that knee extensor activation systematically induced a change in plantar flexor activity in the absence of a change in the mechanical constraint on plantar flexor muscles. The existence of muscle synergies was necessary to explain this phenomenon clearly.

The results presented in Chapter II showed that the dependence on muscle synergies is clearer with low-intensity plantar flexion than with high-intensity plantar flexion; therefore, the aim of the studies reported in Chapter III was to reveal ways in which muscle synergies are recruited at low-intensity plantar flexion. Chapter III is divided into two sections. The results of the study presented in Section I were already published (Suzuki et al. 2014), and confirmed that a change in knee extensor activation induced a drastic change in plantar flexor activity during low-intensity plantar flexion. The aim of the study reported in Section II was to resolve the discrepancy between the muscle synergy hypothesis and the uncontrolled manifold hypothesis at the muscle activation level and provide a valuable insight into the recruitment of muscle synergies. To achieve this aim, the study reported in Section II applied the uncontrolled manifold approach to the variability of plantar flexor activity and muscle synergy recruitment during plantar flexion with and without knee extensor activation.

Although the results of the study represented in Chapter II did not show a clear change in activation ratio between plantar flexor muscles at high-intensity plantar flexion, the activity of the soleus and medial gastrocnemius muscles increased with knee extensor activation. Therefore, the aim of the study reported in Chapter IV was to evaluate the effect of the interaction between plantar flexor and knee extensor muscles on the generation of maximum

plantar flexion torque.

Chapter II deals with plantar flexion torques ranging from low to maximum levels, Chapter III is focused on low-intensity plantar flexion, and Chapter IV examines the supramaximal plantar flexion. Chapter V provides a general discussion on the research, and proposes ways in which muscle synergies are recruited.

Chapter II

Plantar flexor activities are non-mechanically constrained with knee extensor activation

Introduction

Humans have about 400 skeletal muscles (Federative Committee on Anatomical Terminology 1998) that provide flexible solutions to various complex movements. This results in a large number of degrees of freedom that must be controlled by the central nervous system (Bernstein 1967). It has been proposed that the central nervous system addresses this problem by combining small modules of muscles (Bouisset et al. 1977; Lee 1984; Sherrington 1906) that are coactivated in a fixed ratio (Kargo and Giszter 2008; Tresch et al. 1999). These modules are referred to as muscle synergies (cf., Todorov and Jordan 2002). A given muscle can belong to more than one synergy, and the activity of a muscle is determined by a linear combination of muscle synergies related to it (d'Avella et al. 2003; Tresch et al. 1999).

This muscle synergy hypothesis has been supported by stimulation (Bizzi et al. 1991; Dimitrijevic et al. 1998; Huntley and Jones 1991; Kargo and Giszter 2008; Mussa-Ivaldi et al. 1994; Tresch et al. 1999) and behavioral (Bouisset et al. 1977; Buchanan et al. 1986; Cappellini et al. 2006; Cheung et al. 2009; Clark et al. 2010; d'Avella et al. 2003; Roh et al. 2011; Takei and Seki 2010; Torres-Oviedo et al. 2006) studies. For example, in the frog, microstimulation of a site in the lumbar spinal cord elicited a leg force pattern that was related to several muscles (Bizzi et al. 1991), and simultaneous stimulation of two spinal sites linearly summed two corresponding sets of leg forces (Mussa-Ivaldi et al. 1994). The findings of the stimulation approach indicate that linear combination of muscle synergies for various movements is physically possible. In a behavioral approach, at elbow flexion, there was a linear relation, which suggested a synergy (Lee 1984), between the activity of the biceps brachii and the

brachioradialis (Bouisset et al. 1977). Moreover, computational decomposition techniques, such as non-negative matrix factorization (NMF), have identified consistent structure in muscle activities across different tasks (Cappellini et al. 2006; d'Avella et al. 2003; Roh et al. 2011; Torres-Oviedo et al. 2006). Based on a linear combination of synergies, various movements can be explained by a relatively small number of patterns.

Despite enormous physiological and behavioral evidence, the muscle synergy hypothesis has been difficult to prove or falsify (Kutch and Valero-Cuevas 2012; Tresch and Jarc 2009). It has been doubted whether the stimulation approach can elicit the complete repertoire of muscle activation patterns (Kutch and Valero-Cuevas 2012). Even though interneurons are available for the synchronous control of multiple muscles, the specific control of single muscles might be learned and used by the motor cortex (Moritz et al. 2008). Of course, the behavioral approach can examine all practical muscle activation patterns, but is affected by mechanical constraints that reduce feasible activation patterns, independent of neural control (Buchanan et al. 1986; Kutch and Valero-Cuevas 2012; Lee 1984; Tresch and Jarc 2009). Partly because of reduction in feasible activation patterns, a criterion unrelated to muscle synergies could lead to a small number of activation ratio between muscles, which is misinterpreted as muscle synergies. For example, previous studies reported that muscle activities during walking were grouped in a synergy-like manner (Cappellini et al. 2006; Clark et al. 2010; Dominici et al. 2011), but such a grouped muscle activity was roughly predicted by walking simulation based on minimizing an objective function, such as the cubed sum of muscle forces divided by the physiological cross-sectional area (Crowninshield and Brand 1981) or the metabolic energy (Anderson and Pandy 2001). Because previous behavioral studies on muscle synergies did not clarify mechanical constraints (e.g., joint torque) in their experimental setups or could not deny the possibility of misinterpretation of grouped muscles activities due to mechanical constraints or a criterion unrelated to muscle synergies, it remains unclear whether muscle synergies are

involved in human voluntary movements. In addition, previous studies on the control of muscles of the index finger reported the counter-examples to the muscle synergy hypothesis (Kutch et al. 2008; Valero-Cuevas et al. 2009). For example, the variability of the index finger force was larger for the anatomically functional direction of an individual muscle than that for the direction to which more than one muscle simultaneously moved the joint, although the muscle synergy hypothesis predicts the larger variability for the latter direction (Kutch et al. 2008). Further evidence is necessary to verify the muscle synergy hypothesis in humans, and this evidence must be obtained in an experiment that distinguish muscle synergies from non-neural muscle activation patterns constrained by the task.

Previous studies have reported that the ratio between synergist activities changed in a constant mechanical task constraint at elbow flexor (Semmler et al. 1999), and knee extensor (Kouzaki et al. 2002; Sjøgaard et al. 1986), and plantar flexor muscles (Sirin and Patla 1987; Tamaki et al. 1998; see Section I of Chapter III). For example, the activity of the medial gastrocnemius (MG) muscle decreased and that of the soleus (Sol) muscle increased when isometric knee extension was added to isometric plantar flexion even though subjects maintained a constant plantar flexion torque (see Section I of Chapter III). Because plantar flexion has one mechanical constraint (plantar flexion torque only) and more than three degrees of freedom (three heads of the triceps surae muscle and other plantar flexor muscles), there are three possibilities: each plantar flexor muscle is independently activated to generate a total plantar flexion torque (zero synergy); the activity of each plantar flexor muscle changes according to only one activation ratio (one synergy suspected to be due to mechanical constraints because of the equality between the number of activation ratios and the number of mechanical constraints); a different plantar flexor synergy is recruited with simultaneous activation of muscles of the knee (more than one synergy, suggesting the very existence of muscle synergies). Therefore, in vivo observation of different muscle coactivation ratios during

plantar flexion with or without knee extension would provide a valuable insight into the muscle synergy hypothesis.

We hypothesized that the activity of each head of the triceps surae would be determined by muscle synergies. To test this hypothesis, we investigated the linear relations between the activity of triceps surae muscles during voluntary isometric plantar flexion performed with and without voluntary isometric knee extension, compared with the number of mechanical constraints (i.e., plantar flexion torque).

Methods

Subjects

Ten male volunteers participated in the experiment. The mean ± standard deviation age, height, and body mass of the subjects was 24.1 ± 3.0 years, 170.5 ± 7.4 cm, and 70.2 ± 12.6 kg, respectively. No subject had any significant medical history or any signs of a neurological disorder. All subjects gave their written informed consent to participate in the study after receiving a detailed explanation of the purposes, potential benefits, and risks associated with participation. The Human Research Ethics Committee at Kanagawa University approved all procedures used in the study.

Torque and electromyography (EMG) recordings

For all trials, the subject lay prone on a flat seat and the legs were secured with straps placed around the hips and the right knee to minimize changes in joint angles (Fig. 1). The knees were fully extended and were supported by pads that elevated the knee to prevent contact between the seat and the electrodes placed over the vastus lateralis (VL) and rectus femoris (RF) muscles. The right ankle was positioned at 0° (neutral) and the right foot was tightly fixed to the plate of a dynamometer (Biodex System 3 or 4, Biodex Medical Systems, Shirley, NY, USA; or Cont-

Rex CH-8046, CMV AG, Zürich, Switzerland). The axis of rotation of the dynamometer was aligned with the anatomical axis of ankle dorsiflexion and plantar flexion. Special care was taken to ensure that the ankle and knee angles were constant throughout the experiment to remove any influence of joint angle on triceps surae EMG (Cresswell et al. 1995).

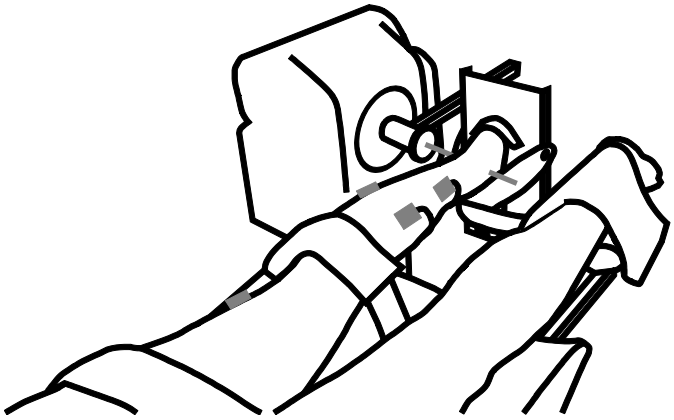

Fig. 1. Experimental setup. The gray line represents the anatomical plantar and dorsiflexion axis. The gray rectangles are electrodes.

Surface EMG was recorded from the VL, RF, gluteus maximus (GM), biceps femoris (BF), tibialis anterior (TA), MG, lateral gastrocnemius (LG), and Sol of the right leg using single differential electrodes (DE-2.1, Delsys, Boston, MA, USA). After carefully abrading and cleaning the skin with alcohol, the electrodes were placed on the skin over the distal part of the VL, RF, and BF muscles, on the skin over the belly of the GM, TA, MG, and LG muscles, and on the skin over the medial aspect of the Sol muscle. The ground electrode was placed on the tuberositas tibiae. The EMG signals were amplified (×100) using a standard biosignal recording system (Bagnoli Desktop EMG Systems, Delsys), and bandpass filtered at 20–450 Hz before sampling. Plantar flexion torque and EMG data were sampled at 2 kHz on the hard disk of a personal computer using a 16-bit analog-to-digital converter (PowerLab 16/30 or 16/35, AD Instruments, Sydney, Australia).

Experimental protocol

The experimental session consisted of maximal voluntary isometric contraction (MVC) trials followed by torque-matching trials in which the subject was required to generate a constant isometric plantar flexion torque while maintaining a constant isometric contraction of the knee

extensors.

Before the experiment, subjects practiced until they could generate the torque as intended. At the beginning of the session, subjects performed MVC trials for hip extension, knee extension, knee flexion, ankle plantar flexion, and ankle dorsiflexion. The level of effort was gradually increased to a maximum to avoid an EMG burst at the start of the contraction. Verbal encouragement was provided for each MVC trial. Each MVC trial lasted >3 s. Two trials were performed for each muscle group. A rest period of a few minutes was provided between consecutive MVC trials. EMG was recorded during all MVC trials, but torque was measured only for the plantar flexion MVC trials. The maximum torque generated during the plantar flexor MVC trials (PFMVC) and the maximum average rectified value (ARV) of the VL EMG during the knee extensor MVC trials (KEMVC) were identified.

After a rest period of a few minutes, subjects performed the torque-matching trials where they were required to generate a constant isometric plantar flexion torque at one of ten levels (10, 20, 30, 40, 50, 60, 70, 80, 90, or 100% PFMVC) while maintaining a constant isometric contraction of the knee extensors at one of three levels (0, 50, or 100% KEMVC). One trial was performed for each condition, giving a total of 30 trials (ten levels of plantar flexion torque × three levels of knee extensor activation) per subject. The plantar flexion torque and knee extensor activation conditions were presented in a random order. Each trial lasted >3 s, and a few minutes of rest was allowed between consecutive trials. The plantar flexion torque, target plantar flexion torque, minimally processed VL EMG, and target VL EMG were displayed in real time on a monitor located in front of the subject. The minimally processed EMG used for feedback purposes was full-wave rectified and low-pass filtered at 10 Hz online using LabChart software (AD Instruments). Subjects were also provided with auditory feedback of the level of knee extensor activity, because it was difficult for them to simultaneously process two forms of visual feedback. If the minimally processed VL EMG was above or below the

target KEMVC by ≥10% KEMVC, the subjects received auditory feedback until the processed signal returned to the target range. At 100% KEMVC, the subjects were encouraged to perform a maximal voluntary knee extension.

Data processing

Post processing of the data was performed using in-house MATLAB algorithms (version 2014a, MathWorks, Natick, MA, USA). For the MVC trials, a 1-s analysis window was moved through the recorded data in 1/2000-s steps. For the ankle plantar flexion MVC trials, torque was averaged over each window. PFMVC torque was defined as the largest of the mean values obtained from all windows over the two trials. The MVC of MG, LG, and Sol was calculated as the ARV in the window in which PFMVC occurred. This analysis depended on the widespread definition that the EMG during the MVC corresponded to the MVC torque in the same moment (Disselhorst-Klug et al. 2009). For the MVC trials for hip extension, knee extension, knee flexion, and ankle dorsiflexion, a 1-s analysis window was moved through the recorded data in 1/2000-s steps and the ARV was calculated over each 1-s window. Because the torque was not measured during the hip extension, knee extension, knee flexion, and ankle dorsiflexion MVC trials, the ARVs of the GM, VL, RF, BF, and TA during MVCs were determined as the largest of the ARVs obtained from all windows over the two MVC trials for each muscle.

For the torque-matching trials, the analysis program identified all 1-s windows where the mean error between the actual plantar flexion torque and the target plantar flexion torque was ≤1% PFMVC, and then identified which of these windows had the minimum difference between actual VL ARV and target VL ARV. In a few cases where VL ARV was quite different from the target, a 1-s window where VL activation was closer to the target level with +1% PFMVC error was identified. The average plantar flexion torque and the ARV of the EMG for

each muscle was calculated over the chosen window and expressed as %MVC.

Two-piece linear regression (TPLR)

The relation between MG and Sol ARV, between LG and Sol ARV, and between LG and MG ARV was not consistent across the range of plantar flexion torques (see Results). As such, these relations were analyzed using TPLR (Quandt 1958). For each level of knee extensor contraction, the relation between the activity of two of the three triceps surae muscles (MG ARV × Sol ARV, LG ARV × Sol ARV, and LG ARV × MG ARV) across the range of plantar flexion torques was fitted with two linear regression lines. Each regression was constrained to fit at least three data points. The breakpoint that minimized the sum of the squared errors between the observed values and the values expected by the regression was identified. The data points from 10% PFMVC to the breakpoint (defined as the lower plantar flexor torques) were fitted with one linear regression and the data points from the breakpoint to 100% PFMVC (defined as the higher plantar flexor torques) were fitted with a second linear regression. The regression coefficients and the coefficients of determination (r^2) were determined for each of the two regression lines.

NMF procedure

The ARV of all muscles were combined into a $m \times r$ matrix (EMG_o), where m indicates the number of muscles (i.e., eight) and r indicates the number of conditions (i.e., 30). For each subject, the NMF algorithm (Lee and Seung 2001) was applied to EMG_o (8 × 30 matrix). The number of synergies, s, was set, and the NMF found the properties of the synergies by populating two matrices: an $8 \times s$ matrix, which specified the relative weighting of muscles in each synergy, and an $s \times 30$ matrix, which specified the recruitment of each synergy in each condition. When these two matrices were multiplied, an 8 × 30 matrix (EMG_r) was produced

that attempted to reconstruct EMG_o. Within this framework, the NMF performed an iterative optimization from various random initial values until it converged on two matrices that minimized the sum of the squared errors: $\sum(EMG_o - EMG_r)^2$.

To determine the minimum number of synergies needed to adequately reconstruct EMG_o, TPLR was applied to the ARV of MG, LG, and Sol in EMG_r with the same breakpoints for those used for the original data (EMG_o). The TPLR revealed significant relations in the ARV of MG, LG, and Sol in EMG_o at the lower plantar flexor torques (i.e., before the breakpoint; see Results), therefore the number of synergies was deemed sufficient when the regression coefficients for the ARV in EMG_r, which were determined by the TPLR, showed the same statistical results as those for EMG_o. To provide an indication of the adequacy of the number of synergies, the variability accounted for (VAF) (Torres-Oviedo et al. 2006) was calculated as the ratio of the sum of the squared EMG_r to the sum of the squared EMG_o: $VAF\ (\%) = 100 \times (\sum EMG_r^2 / \sum EMG_o^2)$.

The local synergies for each subject were clustered into global synergies for all subjects. For each subject, each local synergy was clustered into a different global synergy. The relative weighting of each muscle in each global synergy was the average relative weighting of that muscle in all local synergies contained within that global synergy. Adequate clustering was determined as the clustering that minimized the sum of the squared distance between the recruitment of the global synergy and that of the local synergy clustered into it. The genetic algorithm combined with simulated annealing (Tsoi et al. 1995) was applied to identify adequate clustering. Then, the adequate global synergy set was calculated for this clustering. The recruitment of the global synergy in each condition was the recruitment of local synergies clustered into it.

Statistics

The ARV of VL, MG, LG, and Sol (expressed as %MVC) and the recruitment of each synergy were compared across plantar flexion torques (10, 20, 30, 40, 50, 60, 70, 80, 90, and 100% PFMVC) and knee extensor activation levels (0, 50, and 100% KEMVC) using a two-way analysis of variance with repeated measures. The regression coefficient for MG × Sol, LG × Sol, and LG × MG muscle pairs indicated by the TPLR of EMG_o at the lower and higher plantar flexion torques and the regression coefficient for MG × Sol, LG × Sol, and LG × MG muscle pairs indicated by the TPLR of EMG_r at the lower plantar flexion toques were compared across knee extensor activation levels (0, 50, and 100% KEMVC) using a one-way analysis of variance with repeated measures. Shaffer's post-hoc test was conducted to examine the difference between the knee extension levels. If the interaction between plantar flexion torque and knee extensor activation was significant, post-hoc tests included a multiple comparison for simple effects. The Greenhouse-Geisser degrees of freedom correction (ε) was used to correct for violation of the sphericity assumption. The analysis of variance and post-hoc tests were performed with statistical software (SPSS Statistics 21, IBM Japan, Tokyo, Japan). The effect size (η^2) was calculated by in-house MATLAB algorithms. The level of significance for all comparisons was set at $P < 0.05$.

Results

EMG amplitude

A typical example of the plantar flexion torque and EMG of all muscles during torque-matching contractions at 30% PFMVC is shown in Figure 2. At this low plantar flexion torque (i.e., 30% PFMVC), the MG was tonically active when there was no contraction of knee extensor muscles, but exhibited little activation when isometric knee extension was added to the task. By contrast, Sol EMG increased with contraction of the knee extensors. GM, BF, TA and LG EMG was

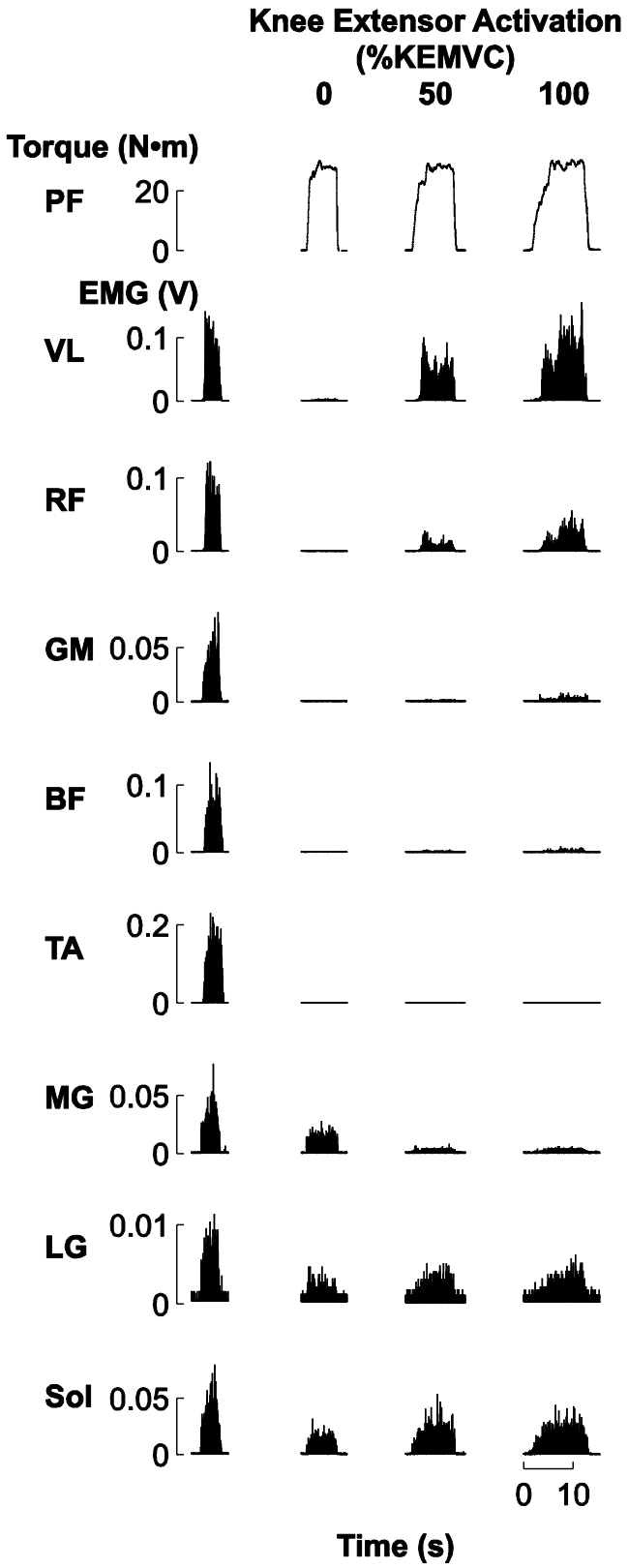

Fig. 2. Example plantar flexion (PF) torque and electromyography (EMG) traces from a representative subject. *Left:* Rectified EMG during a maximal voluntary contraction for each muscle. *Right*: PF torque and rectified EMG during trials in which the subject had to maintain the PF torque at 30% of the maximum voluntary PF torque and the activity of the vastus lateralis (VL) muscle at either 0%, 50% or 100% of maximum. EMG was recorded from the VL, rectus femoris (RF), gluteus maximus (GM), biceps femoris (BF), tibialis anterior (TA), medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (Sol) muscles.

minimal regardless of contraction of the knee extensors. Knee extensor activation therefore seemed to have a particularly strong effect on triceps surae activity. These observations were confirmed in the subsequent analysis of the data from all subjects.

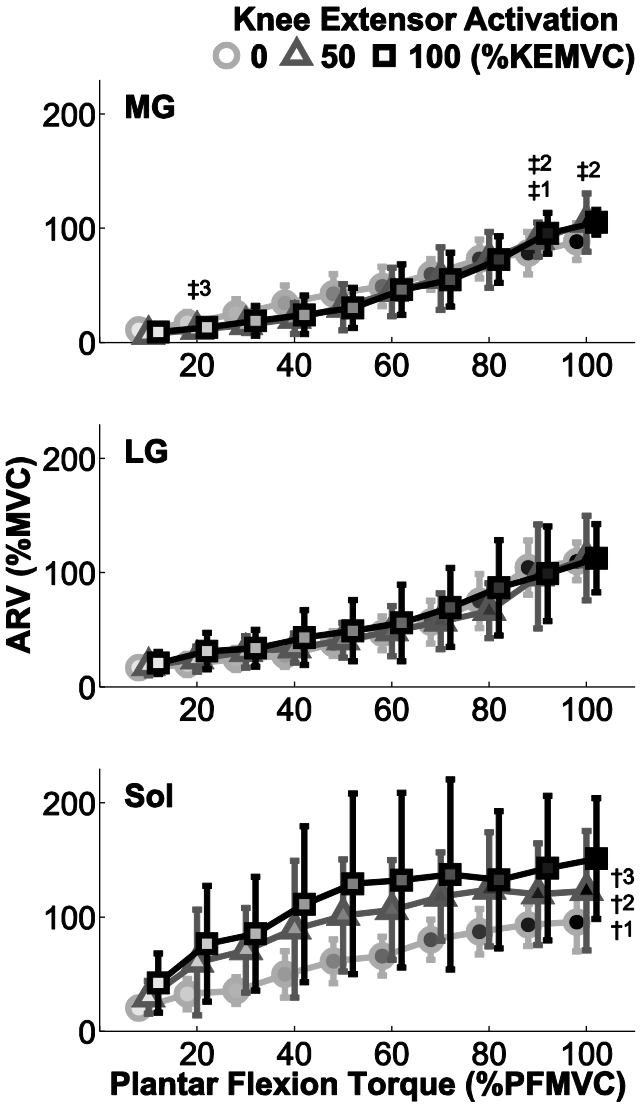

Fig. 3. Average rectified value (ARV) of the electromyographic (EMG) activity of the medial gastrocnemius (MG), lateral gastrocnemius (LG) and soleus (Sol) muscles during the torque-matching trials. The data points indicate the mean and the error bars indicate the standard deviation. Trials were performed with vastus lateralis muscle activity maintained at 0% maximum (0% KEMVC; circles), 50% maximum (50% KEMVC; triangles), or 100% maximum (100% KEMVC; squares). For each muscle, the ARV significantly differed across the plantar flexion torques. PFMVC is the maximum torque generated during the plantar flexion maximal voluntary contraction. The ARV of the EMG is expressed as a percentage of the corresponding value during maximal voluntary contraction (%MVC). Significant differences for main effects are indicated: †1 $P < 0.05$ between 0% and 50% KEMVC; †2 $P < 0.05$ between 0% and 100% KEMVC; †3 $P < 0.05$ between 50% and 100% KEMVC. Significant differences for simple effects are indicated: ‡1 $P < 0.05$ between 0% and 50% KEMVC; ‡2 $P < 0.05$ between 0% and 100% KEMVC; ‡3 $P < 0.05$ between 50% and 100% KEMVC.

The mean error between the target plantar flexion torque and the produced plantar flexion torque was <1% PFMVC for all conditions except 100% PFMVC, where it was <1.5% PFMVC. Regardless of the target plantar flexion torque, VL ARV was about 40% MVC in conditions with a 50% KEMVC target and about 80% MVC in conditions with a 100% KEMVC target. Although VL ARV was lower than the target level, there was a significant main effect of knee extensor activation on VL ARV ($F_{2,18} = 759.9$, $\varepsilon = 0.791$, $\eta^2 = 0.92$, $P < 0.001$), and the post-hoc tests revealed a significant increase in VL ARV from 0% to 50% KEMVC, from 0% to 100% KEMVC, and from 50% to 100% KEMVC ($P < 0.001$ for each comparison).

There was a significant main effect of plantar flexion torque on MG ARV ($F_{9,81} = 162.9$,

$\varepsilon = 0.349$, $\eta^2 = 0.77$, $P < 0.001$) but no effect of knee extensor activation ($F_{2,18} = 0.6$, $\varepsilon = 0.574$, $\eta^2 < 0.01$, $P = 0.602$; Fig. 3). There was a significant interaction between plantar flexion torque and knee extensor activation ($F_{18,162} = 3.2$, $\varepsilon = 0.211$, $\eta^2 = 0.02$, $P = 0.028$). Shaffer's multiple comparison test for simple effects revealed a significant increase in MG ARV from 0% to 50% KEMVC at 90% PFMVC ($P = 0.029$), from 0% to 100% KEMVC at 90% PFMVC ($P = 0.021$) and 100% PFMVC ($P = 0.003$), and from 50% to 100% KEMVC at 20% PFMVC ($P = 0.045$).

There was a significant main effect of plantar flexion torque on LG ARV ($F_{9,81} = 77.0$, $\varepsilon = 0.295$, $\eta^2 = 0.63$, $P < 0.001$) but no effect of knee extensor activation ($F_{2,18} = 2.4$, $\varepsilon = 0.738$, $\eta^2 = 0.01$, $P = 0.136$) and no interaction ($F_{18,162} = 1.0$, $\varepsilon = 0.245$, $\eta^2 = 0.01$, $P = 0.441$; Fig. 3).

There was a significant main effect of plantar flexion torque ($F_{9,81} = 40.8$, $\varepsilon = 0.337$, $\eta^2 = 0.26$, $P < 0.001$) and knee extensor activation ($F_{2,18} = 9.8$, $\varepsilon = 0.508$, $\eta^2 = 0.14$, $P = 0.012$) on Sol ARV, but no significant interaction ($F_{18,162} = 1.6$, $\varepsilon = 0.172$, $\eta^2 = 0.01$, $P = 0.208$; Fig. 3). Shaffer's post-hoc test for main effects revealed a significant increase in Sol ARV from 0% to 50% KEMVC ($P = 0.018$), from 0% to 100% KEMVC ($P = 0.011$), and from 50% to 100% KEMVC ($P = 0.005$).

Coactivation ratio in the triceps surae

A typical scatter plot of MG and Sol ARV across the different plantar flexion torques is shown in Figure 4. At the lower plantar flexion torques (i.e., below the breakpoint), there was a linear relation between the ARV of the two muscles at each level of knee extensor contraction and the slope of the relation differed according to the presence of knee extensor contraction. However, at the higher plantar flexion torques (i.e., after the breakpoint) the slope of any relation did not depend on the level of knee extensor contraction. For the data of all subjects, these patterns were identified by TPLR and the slopes of the relation (i.e., the regression coefficients) were tested.

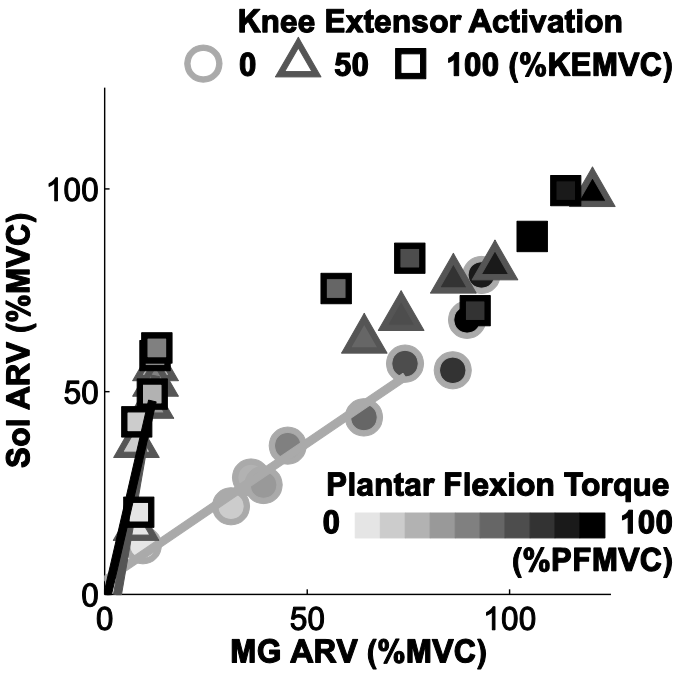

Fig. 4. Example scatter plot of the average rectified value (ARV) of the electromyographic (EMG) activity of the medial gastrocnemius (MG) and soleus (Sol) at different plantar flexion torques. PFMVC is the maximum torque generated during the plantar flexion maximal voluntary contraction. The ARV of the EMG expressed as a percentage of the corresponding value during maximal voluntary contraction (%MVC). The breakpoint is the plantar flexion torque that divides the data points into two groups that are fitted with different linear regressions. The three lines (light grey, dark grey, and black) are the two-piece linear regression lines before the breakpoint for trials performed with vastus lateralis muscle activity maintained at 0% maximum (0% KEMVC; circles), 50% maximum (50% KEMVC; triangles), and 100% maximum (100% KEMVC; squares), respectively. The marker color scale (light grey to black) represents the plantar flexion torque (0% to 100% PFMVC).

At the lower plantar flexion torques, there was a significant main effect of knee extensor activation on the regression coefficient for MG × Sol ($F_{2,18}$ = 10.7, ε = 0.922, η^2 = 0.37, P = 0.001) and LG × MG ($F_{2,18}$ = 7.6, ε = 0.615, η^2 = 0.31, P = 0.015), but no significant main effect on the regression coefficient for LG × Sol ($F_{2,18}$ = 2.7, ε = 0.914, η^2 = 0.06, P = 0.099; Table 1 and Fig. 5, right side: "Observed"). Shaffer's post hoc test for MG × Sol and LG × MG revealed significant differences between 0% and 50% KEMVC (P = 0.003 and 0.028, respectively), and 0% and 100% KEMVC (P = 0.005 and 0.016, respectively), but not between 50% and 100% KEMVC (P = 0.925 and 0.112, respectively). Therefore, at the lower plantar flexion torques, the regression coefficients for these two pairs of the triceps surae muscles significantly differed between 0% KEMVC and the other levels of knee extensor activation.

At the higher plantar flexion torques, the R^2 were lower (Table 1), indicating that the

Table 1. Results of the two-piece linear regression of the activity of pairs of triceps surae muscles.

	%KEMVC	Lower PF torques		Breakpoint (%PFMVC)	Higher PF torques	
		Slope	r^2		Slope	r^2
MG × Sol	0	1.2 (1.0)	0.78 (0.29)	57.0 (9.5)	0.4 (1.2)	0.35 (0.35)
	50	5.2 (3.0)	0.89 (0.17)	49.0 (14.5)	0.0 (0.7)	0.47 (0.39)
	100	5.3 (3.3)	0.88 (0.20)	50.0 (10.5)	0.5 (1.3)	0.46 (0.36)
LG × Sol	0	2.1 (1.3)	0.87 (0.14)	55.0 (14.3)	0.8 (1.9)	0.64 (0.32)
	50	3.1 (2.8)	0.90 (0.18)	56.0 (14.3)	0.2 (0.6)	0.54 (0.38)
	100	3.2 (2.0)	0.92 (0.09)	58.0 (14.0)	0.5 (1.4)	0.51 (0.36)
LG × MG	0	1.3 (0.8)	0.84 (0.18)	60.0 (14.1)	0.4 (0.3)	0.69 (0.36)
	50	0.7 (0.4)	0.81 (0.29)	57.0 (15.7)	0.6 (0.4)	0.68 (0.28)
	100	0.5 (0.3)	0.77 (0.30)	55.0 (13.5)	0.9 (1.2)	0.81 (0.20)

Data are mean (standard deviation) for all subjects. The breakpoint is the plantar flexion (PF) torque that divides the data into two groups (Lower PF torques and Higher PF torques) that were fitted with different linear regressions. MG: medial gastrocnemius; LG: lateral gastrocnemius; Sol: soleus; %KEMVC: target vastus lateralis activity as a percent of maximum; PFMVC: maximum torque generated during the PF maximal voluntary contraction; Slope: regression coefficient; r^2: the coefficient of determination.

linear relation between the two muscles in each pair was weaker. There was no significant main effect of knee extensor activation on the regression coefficient for MG × Sol, LG × Sol, or LG × MG ($F_{2,18}$ = 0.9, ε = 0.847, η^2 = 0.04, P = 0.427; $F_{2,18}$ = 0.4, ε = 0.709, η^2 = 0.02, P = 0.587; $F_{2,18}$ = 1.6, ε = 0.632, η^2 = 0.09, P = 0.232, respectively; Table 1).

Global synergy set

The averages of the TPLR of NMF-reconstructed ARVs at the lower plantar flexion torques (i.e., below the breakpoint) for all subjects are shown in Figure 5 for one, two, three and four synergies (left side; "Reconstructed"). Of course, the regression line was the same as the line of identity when the number of synergies was one. Two synergies resulted in three regression lines with similar slopes. Three synergies resulted in two regression lines for MG × Sol, similar to the observed relations, which are illustrated on the right side of Figure 5 (right side: "Observed"), but the lines were close to parallel and nearly overlapping for LG × MG. When the number of synergies was four, the slopes of the regression lines for the reconstructed data appeared similar

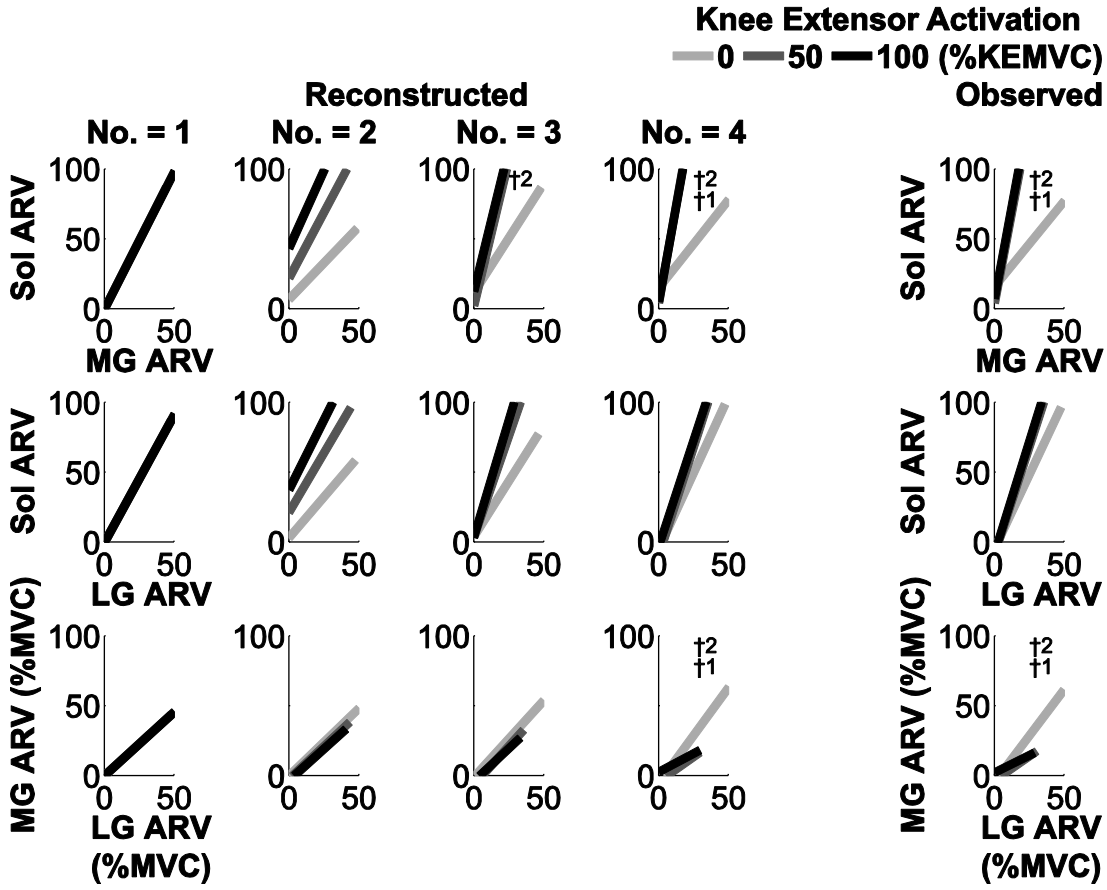

Fig. 5. The mean regression lines for the average rectified value (ARV) of medial gastrocnemius (MG) and soleus (Sol) electromyographic (EMG) activity (top row), lateral gastrocnemius (LG) and Sol EMG activity (middle row), and LG and MG EMG activity (bottom row) at lower plantar flexion torques for trials performed with vastus lateralis muscle activity maintained at 0% maximum (0% KEMVC; light grey), 50% maximum (50% KEMVC; mid-grey), and 100% maximum (100% KEMVC; black). The mean regression lines for all subjects are shown from data reconstructed with one synergy (No. = 1), two synergies (No. = 2), three synergies (No. =3), four synergies (No. = 4), and from original data (Observed). The ARV of the EMG is expressed as a percentage of the corresponding value during maximal voluntary contraction (%MVC). Significant differences are indicated: †1 $P < 0.05$ between 0% and 50% KEMVC; †2 $P < 0.05$ between 0% and 100% KEMVC.

to those for the original data. The mean ± standard deviation VAF was 88.2 ± 2.9, 97.3 ± 0.9, 99.2 ± 0.3, and 99.7 ± 0.2 %, for one, two, three, and four synergies, respectively.

For MG × Sol and LG × MG, the regression coefficient from the TPLR of EMG_r at the lower plantar flexion torques was compared across the levels of knee extensor activation using Shaffer's multiple comparison test. Three synergies could not sufficiently reconstruct the significant differences between 0% KEMVC and the other levels of knee extensor contraction

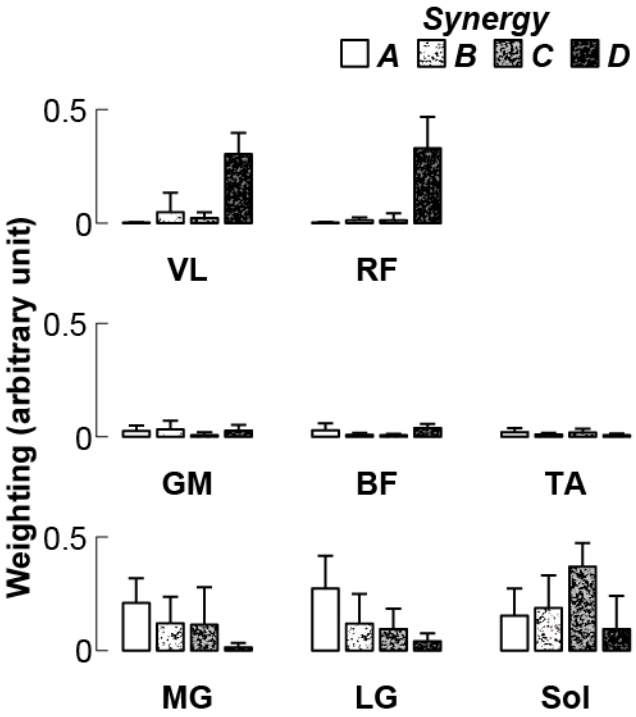

Fig. 6. Global synergy set. The average rectified values of the electromyographic activity of all muscles for each subject were decomposed into a synergy-weighting matrix and a recruitment matrix using non-negative matrix factorization. Each global synergy is the mean weighting of all subjects' synergies clustered into it. The values shown are the weightings of the vastus lateralis (VL), rectus femoris (RF), gluteus maximus (GM), biceps femoris (BF), tibialis anterior (TA), medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (Sol) muscles in each global synergy. The error bars indicate standard deviation.

observed in the original data (Fig. 5). After four synergies were applied, all statistical results for the regression coefficients of the reconstructed data were the same as those for the regression coefficients of the original data. Therefore, the adequate number of synergies was determined to be four. Then, the adequate global synergy set was calculated.

Recruitments of muscle synergies

The four synergies were defined as *Synergy A*, *B*, *C*, and *D*. Figure 6 shows the relative weighting of each muscle in each of the four synergies. *Synergy A* involves a high weighting for all three of the triceps surae, indicating that the recruitment of *Synergy A* leads to coactivation of the MG, LG, and Sol with little activation of the VL, RF, GM, BF, and TA. When the recruitment of a certain synergy increases several fold, each muscle activity also increases several fold according to its weighting in the synergy. The recruitment of each synergy for each of the 30 combinations of plantar flexion torque and knee extensor activation is presented in Figure 7.

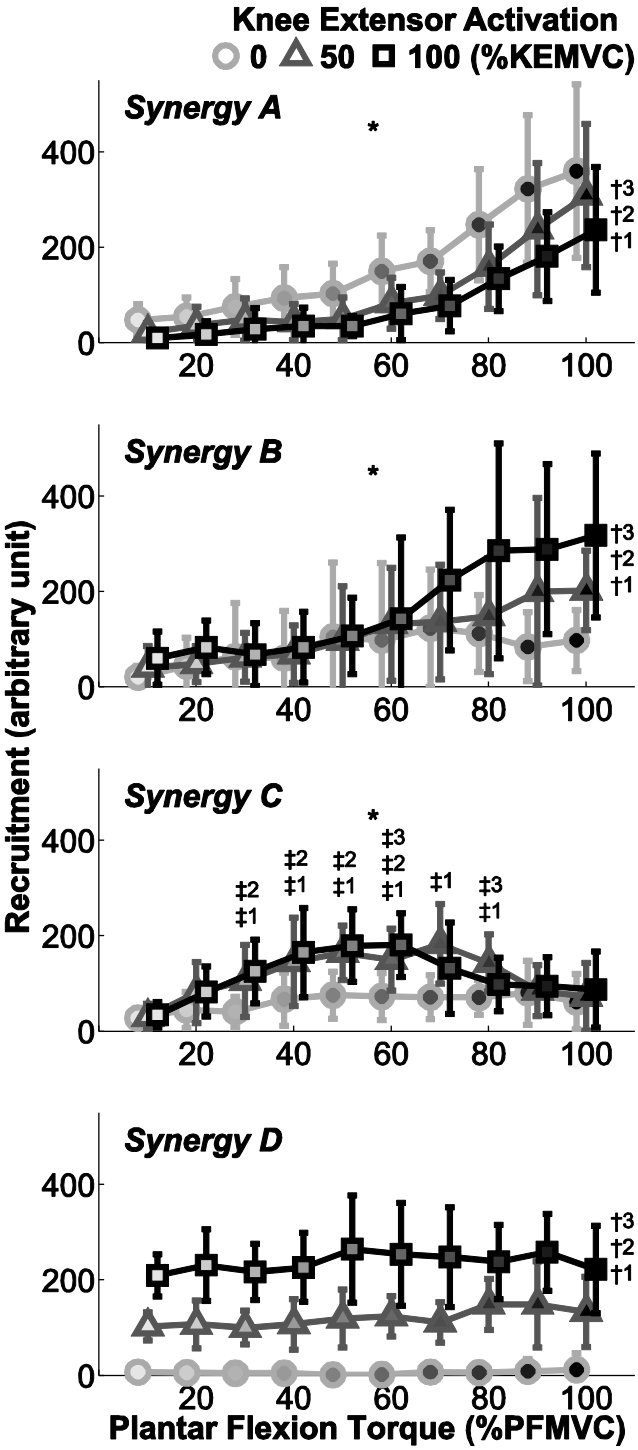

Fig. 7. The recruitment of *Synergy A*, *Synergy B*, *Synergy C* and *Synergy D* during the torque-matching trials. The data points indicate the mean and the error bars indicate the standard deviation. Trials were performed with vastus lateralis muscle activity maintained at 0% maximum (0% KEMVC; circles), 50% maximum (50% KEMVC; triangles), or 100% maximum (100% KEMVC; squares). PFMVC is the maximum torque generated during the plantar flexion maximal voluntary contraction. Significant differences for main effects are indicated: * $P < 0.05$ among the plantar flexion torques; †1 $P < 0.05$ between 0% and 50% KEMVC; †2 $P < 0.05$ between 0% and 100%; †3 $P < 0.05$ between 50% and 100%. Significant differences for simple effects are indicated: ‡1 $P < 0.05$ between 0% and 50% KEMVC; ‡2 $P < 0.05$ between 0% and 100% KEMVC; ‡3 $P < 0.05$ between 50% and 100% KEMVC.

In *Synergy A*, the weightings of MG and LG were greater than the weighting of Sol (Fig. 6). The recruitment of *Synergy A* significantly differed across plantar flexion torques ($F_{9,81}$ = 29.6, ε = 0.177, η^2 = 0.53, $P < 0.001$) and knee extensor activation levels ($F_{2,18}$ = 15.7, ε = 0.600, η^2 = 0.07, P = 0.002; Fig. 7). There was no interaction between plantar flexion torque and knee extensor activation ($F_{18,162}$ = 1.5, ε = 0.207, η^2 = 0.02, P = 0.217). Shaffer's post-hoc

test for main effects revealed a significant decrease in the recruitment of *Synergy A* from 0% to 50% KEMVC ($P = 0.005$), 0% to 100% KEMVC ($P = 0.002$), and 50% to 100% KEMVC ($P = 0.007$).

Synergy B also represented the triceps surae, but its largest contributor was Sol (Fig. 6). The recruitment of *Synergy B* significantly differed across plantar flexion torques ($F_{9,81} = 9.5$, $\varepsilon = 0.216$, $\eta^2 = 0.19$, $P = 0.002$) and knee extensor activation levels ($F_{2,18} = 15.7$, $\varepsilon = 0.570$, $\eta^2 = 0.07$, $P = 0.002$; Fig. 7). There was no interaction between plantar flexion torque and knee extensor activation ($F_{18,162} = 2.9$, $\varepsilon = 0.126$, $\eta^2 = 0.02$, $P = 0.070$). Shaffer's post-hoc test for main effects revealed a significant increase in the recruitment of *Synergy B* from 0% to 100% KEMVC ($P = 0.002$) and from 50% to 100% KEMVC ($P < 0.001$).

Synergy C was similar to *Synergy B* in that it represented the triceps surae, and its largest contributor was Sol (Fig. 6). The recruitment of *Synergy C* significantly differed across plantar flexion torques ($F_{9,81} = 8.9$, $\varepsilon = 0.376$, $\eta^2 = 0.19$, $P < 0.001$) and knee extensor activation levels ($F_{2,18} = 15.6$, $\varepsilon = 0.603$, $\eta^2 = 0.12$, $P = 0.002$), and there was a significant interaction between plantar flexion torque and knee extensor activation ($F_{18,162} = 3.1$, $\varepsilon = 0.217$, $\eta^2 = 0.07$, $P = 0.028$; Fig. 7). Shaffer's post-hoc test for simple effects revealed that the recruitment of *Synergy C* significantly differed between 0% and 50% KEMVC at 30%, 40%, 50%, 60%, 70%, and 80% PFMVC ($P = 0.020$, 0.012, 0.042, 0.009, 0.018, and 0.006, respectively), between 0% and 100% KEMVC at 30%, 40%, 50%, and 60% PFMVC ($P = 0.006$, 0.018, 0.019, and 0.003, respectively), and between 50% and 100% KEMVC at 60% and 80% PFMVC ($P = 0.046$ and 0.019, respectively).

Synergy D had high weightings for the VL and RF and low weightings for the triceps surae (Fig. 6). The recruitment of *Synergy D* significantly differed according to knee extensor activation ($F_{2,18} = 130.7$, $\varepsilon = 0.581$, $\eta^2 = 0.01$, $P < 0.001$) but did not differ across plantar flexion torques ($F_{9,81} = 1.8$, $\varepsilon = 0.275$, $\eta^2 = 0.72$, $P = 0.177$; Fig. 7). There was no interaction between

plantar flexion torque and knee extensor activation ($F_{18,162}$ = 1.3, ε = 0.224, η^2 = 0.01, P = 0.286). Shaffer's post-hoc test for main effects revealed a significant increase from 0% to 50% KEMVC, from 0% to 100% KEMVC, and from 50% to 100% KEMVC (all $P < 0.001$).

Discussion

Influence of knee extensor activation on the coactivation ratio in the triceps surae

The main findings of the present study were that the presence of knee extensor activation changed the linear relation between MG and Sol activity at low plantar flexion levels and changed the recruitment of plantar flexor synergies extracted by the NMF. These findings suggest the existence of multiple plantar flexor synergies, which are selectively recruited during human voluntary movements, depending on the task.

At the lower plantar flexion torques, linear regressions fitted well to the data points (r^2 > 0.75; Table 1). When the knee extensors were not contracting, the activity of MG, LG, and Sol, which was expressed as %MVC, increased as plantar flexion torque increased, and the activity of all three muscles increased at a similar rate. Simultaneous contraction of the knee extensor muscles induced a different ratio of coactivation in the triceps surae, whereby, at the lower plantar flexion torques, the activity of Sol increased much faster than the activity of MG (Fig. 3) as plantar flexion torque increased, as indicated by a slope of 5.8 for the relation between MG and Sol activity. In the presence of knee extensor activity, the slope of the relation between MG and Sol was four-times as large as that in the absence of knee extensor activity (Table 1). Therefore, activation of the knee extensors served as a trigger to change the linear relation between the triceps surae muscles during plantar flexion.

Because the ratio of activity in the triceps surae was influenced by knee extensor activity, the activity of each triceps surae muscle was greatly affected by knee extensor activity. Because MG and Sol activity depended on the steeper regression line for the relation between

these activities at the lower plantar flexion torques (Fig. 5), Sol activity increased almost twofold at a given plantar flexion torque as knee extensor activation increased from 0% to 100% KEMVC (Fig. 3).

The knee-extensor-induced change in the linear relation between the activities of plantar flexor muscles at the lower plantar flexion torques required at least two plantar flexor synergies. If one synergy was heavily weighted for triceps surae activity and the other synergy that partly expressed the heteronymous facilitation pathways between the quadriceps and triceps surae muscles (Meunier et al. 1993) was weighted for the knee extensors and triceps surae, the regression line for the activity of any two of the three triceps surae would be parallel-shifted when the knee extensors were activated, because a certain level of knee extensor activation would always generate a corresponding increase in triceps surae activity, similar to the results for two synergies shown in Figure 5. In this case, these two synergies result in not two but three regression lines because increasing knee extensor contraction level from 50% to 100% KEMVC recruited the synergy that was heavily weighted for the knee extensors and the triceps surae, and increased triceps surae activity along with knee extensor activity. Only after two synergies for the triceps surae (*Synergies A* and *B* in this study) and one synergy for the knee extensors (*Synergy D* in this study) were applied could two regression lines and the drastic change between the slopes of these lines be duplicated. Because knee extensor contraction at the fully extended position did not generate external force and maintained the mechanical task constraints for the plantar flexor muscles, the observed number of plantar flexor synergies should be one if mechanical constraints determined the grouped muscle activity that would be misinterpreted as a muscle synergy. Because the number of constrained muscle activation patterns exceeded the number of mechanical constraints, the requirement of more than one plantar flexor synergy to explain the phenomenon proves the existence of muscle synergies, which are non-mechanical constraints.

The NMF confirmed the important influence of knee extensor activation on plantar flexor activation patterns, similar to the regression analysis. *Synergy A* and *Synergy B* had high weights for the triceps surae muscles. The recruitment of these synergies significantly increased with increasing plantar flexion torque (Fig. 7), resulting in an increase in the activity of the triceps surae muscles (Fig. 3). With an increase in knee extensor activation, the recruitment of *Synergy B* significantly increased, and the recruitment of *Synergy A* significantly decreased (Fig. 7). This is an example of synergy switching due to knee extensor activity. Because *Synergy B* had a larger weighting for the Sol relative to the MG and LG than *Synergy A* (Fig. 6), the slope of regression between MG and Sol activity became more vertical with activation of the knee extensors (Fig. 3 and the right-most column of Fig. 5). The recruitment of *Synergy C* significantly increased with knee extensor activation at some low plantar flexion torques, and this explained the twofold increase in Sol activity observed in the presence of knee extensor activation at the lower plantar flexion torques (Fig. 3).

Physiological mechanism

The size principle that motoneurons are recruited in an orderly manner from small to large (Henneman et al. 1965) allows a better understanding of the physiological mechanism of the linearity in the muscle synergy hypothesis. Motoneurons innervating a given muscle would be divided into so-called task groups (Loeb 1985), and the size principle is held within each task group (Riek and Bawa 1992). A task group would be formed across muscles, and mixed motoneurons of different task groups are not recruited in an orderly manner during simultaneous activation of various task groups (Sokoloff et al. 1999; Wyman et al. 1974). Motoneurons innervating multiple muscles can be connected by a spinal interneuron (Bizzi et al. 1991; Takei and Seki 2010) or a cortical interneuron through corticomotoneuronal cells (Huntley and Jones 1991), and these interneurons could form a task group across multiple muscles. Within the

framework of the size principle, a muscle synergy could be expressed as such a task group. The recruitment of motoneurons in a given muscle synergy depends on the size principle, and muscles are linearly activated according to the size of motoneurons within a muscle synergy, although the firing rate (Adrian and Zotterman 1926) should also be considered. Based on the dependence of individual muscle synergies on the size principle, linear muscle activation and linear summation of activation, which have been premised by the muscle synergy hypothesis (Bizzi et al. 1991; Mussa-Ivaldi et al. 1994; Tresch et al. 1999) or the NMF (Lee and Seung 2001), are implementable for the physiological systems of motor control.

In this study, such an activation linearity was clearly indicated as two regression lines between the activity of the MG and Sol at the lower plantar flexion torques (Fig. 5). Invasive studies have revealed that individual muscles, which can belong to multiple muscle synergies, are collectively controlled by interneurons in animals such as the frog (Bizzi et al. 1991; Mussa-Ivaldi et al. 1994) and the monkey (Huntley and Jones 1991; Takei and Seki 2010). Because of the difficulty of using invasive approaches in humans, behavioral approaches are necessary for studies on synergy recruitment strategy in human voluntary movements. Although the relation between muscle synergies and interneurons remains unclear in human voluntary contractions, this behavioral study revealed that muscles were collectively activated and there was a switching in the linear relation between synergist activities, which could reflect muscle synergies, according to the task in humans.

Comparison with previous studies

Many previous behavioral studies on muscle synergies aimed to show that a small number of muscle synergies could explain a large number of muscle activation patterns under various mechanical constraints on several human voluntary movements (Cappellini et al. 2006) or various phases of a task (Clark et al. 2010; Dominici et al. 2011). However, these studies did

not clarify the number of mechanical constraints (e.g., joint torque) in their movements. If various movements or phases of a task have similar time-series data of a joint torque, a small number of muscle synergies roughly accounts for only a small number of muscle activation patterns depending on mechanical constraints. In this situation, the number of muscle synergies is similar to the number of mechanical constraints, and then, extracted muscle synergies result from misinterpretation of grouped muscle activities induced by mechanical constraints. In addition, a criterion unrelated to muscle synergies could lead to a small number of activation ratio between muscles, which is also misinterpreted as muscle synergies. For example, computer simulation that was based on minimizing an objective function such as the cubed sum of muscle forces divided by the physiological cross-sectional area (Crowninshield and Brand 1981), muscle activation (Kaufman et al. 1991), or the sum of metabolic energies (Anderson and Pandy 2001), with no assumption as to muscle synergies tends to predict the balanced activity of synergists because load concentration to one muscle increases these objective functions, although the fiber length, contraction velocity, and moment arm of muscles influence the prediction of muscle activities. The balanced activity of synergists through time-series data of a joint torque seemingly suggests that these synergists are activated in a nearly fixed ratio (Anderson and Pandy 2001; Crowninshield and Brand 1981; Kaufman et al. 1991), having a risk of misinterpretation as muscle synergies. Therefore, even if a small number of muscle synergies could explain muscle activities during various voluntary movements, it remains unclear whether muscle synergies determine muscle activities, or not (i.e., mechanical constraints or the above-mentioned criterions for computer simulation induce grouped muscle activity in a nearly fixed ratio).

This study aims to show that multiple muscle synergies exist even in a small number of mechanical constraints. If each muscle is independently activated to one mechanical constraint (i.e., plantar flexion torque), the number of extracted plantar flexor synergies should

be one. In this study, the number of plantar flexor synergies exceeded that of mechanical constraints (Figs. 5 and 6), suggesting that the activity of plantar flexor muscles is non-mechanically constrained. Because the constant posture in a non-fatigue state (cf., Sirin and Patla 1987; Tamaki et al. 1998) did not change the length of muscle-tendon complex and moment arm of plantar flexor muscles (cf., Cresswell et al. 1995) in this study, the above-mentioned criterions for computer simulation could not predict this exceeded number of muscle synergies. Therefore, more than one plantar flexor synergy extracted in the present study confirms that muscle synergies are involved in the human voluntary lower limb control.

Previous studies reported that activation of knee muscles was affected by the activity of hip muscles, and activation of each muscle could be approximated by summation of the knee extension (flexion) torque multiplied by an individual constant and the hip extension (flexion) torque multiplied by another individual constant (Nozaki et al. 2005a, 2005b). Although it is possible that the activity of plantar flexor muscles could also be predicted by linear combination of plantar flexion torque and knee extension torque, there was a significant interaction at MG activity between plantar flexion torque and knee extensor activation in the present study (Fig. 3). Especially, the activity of the MG that acts as a knee flexor muscle should have a negative constant related to the knee extension torque but increased with knee extensor activation during high-intensity plantar flexion. These results suggest that the relation between the plantar flexion torque and MG activity was changed by knee extensor activation and linear combination of plantar flexion torque and knee extension torque could not predict MG activation. Moreover, the slope of regression lines between MG and Sol activities was changed by the presence of knee extensor activation (Fig. 5). If MG and Sol activities had individual constants related to the plantar flexion torque, knee extensor activation would not induce this change of slope. Because the other joint torques (e.g., ankle inversion torque) could not be estimated in this study, plantar flexor activities would have constants related to these joint torques, and linear

combination including these joint torques might be able to reconstruct the observed change in a clear regression line. Taking reconstruction of regression lines into account, such a joint torque during knee extensor activation should proportionally increase with increasing plantar flexion torque (cf., *Synergy C* in Fig. 7) although this joint torque should not be proportional to the plantar flexion torque during plantar flexion alone. In contrast to this restrictive assumption, it is reasonable that recruited muscle synergies are changed by knee extensor activation and the recruitment of these muscle synergies (e.g., *Synergy C*) increases to generate a targeted plantar flexion torque. Although the activity of plantar flexor muscles could be predicted by linear combination of muscle synergies rather than joint torques, future studies based on simultaneous calculation of various knee and ankle joint torques are necessary to examine the predictability of linear combination of ankle and knee joint torques for plantar flexor activities.

Difference between upper and lower limb control

Previous studies on counter-examples to the muscle synergy hypothesis evaluated the index finger (Kutch et al. 2008; Valero-Cuevas et al. 2009), which required fine tune control. Even though specific control of individual muscles without muscle synergies increases the amount of calculation, the flexibility of specific control is suitable for the finger. Morphological studies suggested that corticomotoneuronal connections provided a part of the neural substrate for the manual dexterity (Bortoff and Strick 1993; Costello and Fragaszy 1988). Compared to the squirrel monkey, which could not perform independent movements of the fingers, the cebus monkey, which could do it regardless of its similar mobility of joints in the wrist or hand (Costello and Fragaszy 1988), had abundant corticomotoneuronal connections (Bortoff and Strick 1993). The muscles of human fingers might be specifically controlled by the primary motor cortex not through spinal interneurons, which likely compose a large part of muscle synergies (Bizzi et al. 1991; Mussa-Ivaldi et al. 1994; Roh et al. 2011; Takei and Seki 2010),

but through corticomotoneuronal connections.

In contrast to the finger, the primary responsibility of the lower limb, including the ankle, is locomotion, where plantar flexor muscles are mainly used for the force generation. The dynamical systems approach indicated the possibility that the relatively simple control laws could accomplish a stable locomotion by combination of a small number of modules (Taga et al. 1991). Therefore, simplification of control of multiple muscles by muscle synergies is suitable for the lower limb control. The dependence of plantar flexor activities on muscle synergies in the present study would reflect such a characteristic of lower limb muscles.

Limitations

Three plantar flexor synergies were needed according to the criterion for determination of the number of muscle synergies in this study (Fig. 5), and this resulted in a high VAF (99.7%). Two plantar flexor synergies seemed to reconstruct two regression lines (Fig. 5), and resulted in a VAF of 99.2%. Previous studies where the criterion was arbitrarily set (e.g., VAF >90%) have reported that even one plantar flexor synergy can explain the activities of plantar flexor muscles during human walking to some extent (Cappellini et al. 2006; Clark et al. 2010; Dominici et al. 2011). However, previous studies have reported that planar flexor activities change with a posture (Cresswell et al. 1995) and muscle contraction velocity (Moritani et al. 1991). A change in a knee joint angle affected the force-EMG relation of plantar flexor muscles (Cresswell et al. 1995), which might reflect altered recruitment of plantar flexor synergies. The ratio of MG activity to Sol activity increased with increasing demand of force and speed during quick or forceful hopping (Moritani et al. 1991). Moreover, for a human arm aiming task, a recent simulation study predicted that the number of muscle synergies extracted by the NMF with VAF of either 90% or 98% was enough to roughly reconstruct given muscle activities but not enough to accomplish a given performance (de Rugy et al. 2013). Taking these findings into account,

previous studies based on a threshold of about 90% VAF have disregarded the variety of plantar flexor activation patterns and would have overlooked multiple plantar flexor synergies. A high VAF is necessary to explain plantar flexor activation, and the criterion that selects the minimum number of synergies to explain a given phenomenon is useful and not arbitrary.

The criterion in this study was stringent and required three plantar flexor synergies that were extracted by the NMF, although two plantar flexor synergies seemed to reconstruct two regression lines (Fig. 5). The number of plantar flexor synergies was equal to the number of recorded plantar flexor muscles, undoubtedly proving that the number of plantar flexor synergies was not one, but somewhat obscuring whether zero or more than one synergy existed. However, the NMF combined the weightings of the triceps surae muscles into three plantar flexor synergies because these combinations lead to better reconstruction of the low activity of other muscles than three independent weightings for the individual triceps surae muscle (Fig. 6). In addition, independent activity of triceps surae muscles could not explain two clear regression lines (Fig. 4 and the right of Fig. 5). If triceps surae muscles were independently activated, the data points were sparsely scattered with no structure. Two clear regression lines indicated that triceps surae activities were constrained in at least two structures, which exceeded the number of mechanical constraints. Although the criterion in this study might have been too stringent to extract three plantar flexor synergies, it can be emphasized that at least two plantar flexor synergies were notionally needed for two regression lines, and this finding suggests the existence of muscle synergies, which are non-mechanical constraints.

In another aspect, the equality between the number of muscle synergies and the number of recorded muscles does not indicate dimensionality reduction, which is one of the assumed significances of muscle synergies (d'Avella et al. 2003; Tresch et al. 1999, 2009). The activity of plantar flexor muscles other than triceps surae was not recorded, and future studies are required to determine whether the number of muscle synergies is more than the number of task

constraints but less than the number of related muscles, resulting in dimensionality reduction.

Conclusions

The present study revealed that the linear relation between the activity of the three triceps surae muscles drastically changed with knee extensor activation at the constant plantar flexion torque. This finding provides the first behavioral evidence that muscle synergies undecided by mechanical task constraints are selectively recruited during human voluntary movements depending on the task.

Section I of Chapter III

Gastrocnemius and soleus are selectively activated when adding knee extensor activity to plantar flexion

Introduction

Most activities of daily living involve multi-joint movements. For example, simultaneous motions of ankle and knee joints are required for many activities, including standing (Horak and Nashner 1986), running (Duysens et al. 1991), swimming (Troup 1999), and cycling (Andrews 1987; De Marchis et al. 2013). During these multi-joint movements, biarticular muscles, such as the gastrocnemius, have direct effects on two joints at the same time (Lombard 1903), and these effects depend on task constraints, including the movement direction, joint displacement, and external force (Andrews 1987; Zajac 1993). Therefore, control of biarticular muscles is complex and important to multi-joint movements.

The gastrocnemius, a biarticular muscle that crosses the ankle and knee, functions as both a plantar flexor and a knee flexor. Partly because of this anatomical characteristic, the muscle activation level of the gastrocnemius increases when voluntary knee flexion is added to voluntary isometric plantar flexion (Gravel et al. 1987). However, in a situation where both plantar flexion and knee extension are required, it is possible that the activity of the gastrocnemius, which is an antagonist during knee extension, would be depressed. Such depression of antagonist activity is induced by agonist activity through neural pathways, an action called reciprocal inhibition. This well-known phenomenon has been carefully investigated in the ankle (Nielsen and Pierrot-Deseilligny 1996) and elbow (Katz et al. 1991). Previous studies, however, had little concern about reciprocal inhibition at the human knee (Bayoumi and Ashby 1989; Hamm and Alexander 2010; Kudina 1980), and they did not deal with the gastrocnemius as a knee flexor. Therefore, it is unclear how voluntary activation of

knee extensors influences gastrocnemius activity. If activation of knee extensors causes gastrocnemius activity to decrease while satisfying the total demand of plantar flexion torque, the activities of monoarticular plantar flexors, such as the soleus (Sol), are increased, changing the load share among plantar flexors.

In this study, it was hypothesized that gastrocnemius activity is depressed and Sol activity is increased during simultaneous motion of plantar flexion and knee extension. To test this hypothesis, we investigated activation of triceps surae when voluntary isometric knee extension was added to voluntary isometric plantar flexion.

Methods

Subjects

Ten male volunteers participated in the experiment. Their ages, heights, and body masses (mean ± SD) were 25.3 ± 3.6 years, 173.0 ± 5.3 cm, and 68.2 ± 8.7 kg, respectively. They had no medical history or signs of a neurological disorder. All subjects gave their written informed consent for the study after receiving a detailed explanation for the purposes, potential benefits, and risks associated with participation in the study. The Human Research Ethics Committee at the Department of Life Sciences, The University of Tokyo, approved all of the procedures used in the study.

Force and electromyography recordings

For all of the trials, each subject was required to maintain a prone posture with no joint angle changes. A knee was fully extended on a bed with pads that elevated the knee to avoid contact of the bed with the electrode on the rectus femoris (RF). The ankle was fixed at 0° (neutral position), and the right foot was tightly strapped to a plate of a dynamometer (VTF-002; VINE

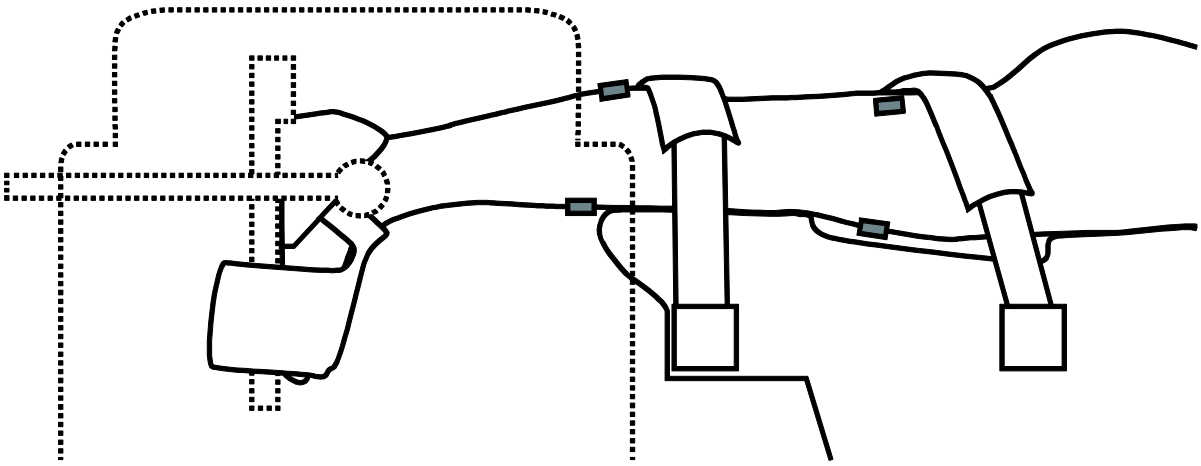

Fig. 1. Experimental setup. The broken lines represent the dynamometer. The gray rectangles are electrodes.

Bionic Systems, Tokyo, Japan) with a strain gauge (LTZ-500KA; Kyowa, Tokyo, Japan) amplified by a strain amplifier (CDV-700A; Kyowa) or a torque-measuring system (Biodex System 3; Biodex Medical Systems, Shirley, NY, USA) (Fig. 1). The angles of the right ankle and knee were carefully fixed to remove any influence of angular variations on the electromyography (EMG) tracings of the triceps surae (Cresswell et al. 1995). The constancy of the knee angle was checked by a goniometer (SG150; Biometrics, Gwent, UK) for seven subjects, and the goniometer was taken off to immobilize the knee as strictly as possible for three subjects. In the pilot study, we had confirmed that isometric knee extension with no plantar flexor activation had no effect on the torque signal of the present experimental setup.

Surface EMGs were recorded from the RF, biceps femoris (BF), tibialis anterior (TA), MG, lateral gastrocnemius (LG), and Sol using two Ag-AgCl electrodes with diameters of 10 mm and an inter-electrode distance of 20 mm. After carefully abrading and cleaning the skin with alcohol, the electrodes were placed over distal parts of the RF and BF; the bellies of the TA, MG, and LG; and a medial protrusion of the Sol. The ground electrode was placed on the tuberositas tibiae. The EMG signals were amplified using a standard biosignal recording system (model 365, NEC Medical Systems, Tokyo, Japan; or Bagnoli Desktop EMG Systems, Delsys, Boston, MA, USA), with filtering at a bandwidth of 5 Hz to 1 kHz. All electrical signals were stored with a sampling frequency of 2 kHz on the hard disk of a personal computer using a 16-

bit analog-to-digital converter (PowerLab 16/30; ADInstruments, Sydney, Australia).

Experimental protocol and data analyses

Before the experiment, the subjects practiced until they could generate the targeted torque. For the maximum voluntary contraction (MVC) trials, they performed isometric MVCs for knee extension, knee flexion, plantar flexion, and dorsiflexion. They gradually increased the contraction level to a maximum to avoid a short-time burst on the EMG at the initial rise. Each trial lasted for > 3 s and was conducted twice. Rest periods between trials lasted a few minutes. The EMGs were recorded during all trials, but torque was measured only for plantar flexion.

The data obtained during the MVC trials were processed as follows. The 1-s analyzed window was moved through the recorded time in 1/2000-s steps. For the MVC trial of plantar flexion, the torque was averaged over each window. The maximum voluntary isometric plantar flexion (PFMVC) torque was defined as the largest among all the mean torque values obtained from all of the windows of two trials. The average rectified values (ARVs) of the EMGs of the MG, LG, and Sol were calculated at the same window where the PFMVC was obtained. This analysis depended on the widespread definition that the EMG during the MVC corresponded to the MVC torque in the same moment (Disselhorst-Klug et al. 2009). For the above-mentioned MVC trial for knee extension, knee flexion, or dorsiflexion, the 1-s window was shifted in 1/2000-s steps, and the ARV was calculated over each 1-s window. Because the produced torques were not measured during the MVC trials (except for plantar flexion), the ARVs of the RF, BF, and TA during MVCs were determined as the largest among the ARVs obtained from all windows of two MVC trials for each muscle.

After a rest period of a few minutes following the MVC trials, the subjects undertook the main trials. They performed constant isometric plantar flexion at 10%, 20%, and 30% of the PFMVC (%PFMVC), in random order. These levels were chosen because almost all bursts of

triceps surae EMG activity were less than 30% MVC in activities of daily living (Shirasawa et al. 2009). The resulting plantar flexion torque and target torque levels were displayed on an oscilloscope in front of the subject to provide visual feedback. They performed each plantar flexion once at each level. They were asked to set the plantar flexion torque as close as possible to the target level during the first 15 s. After the first 15 s, they were asked to add knee extensor activity to the plantar flexion. The knee extension levels were set at 0%, 50%, and 100% of the maximum voluntary isometric knee extensor activation (%KEMVC). They were asked to press a plate in a same manner at all knee extension conditions. Because the root mean square value of the EMG of the RF was proportional to the knee extension torque at any portion of the muscle (Watanabe et al. 2012), the KEMVC was determined not by the torque but by RF ARV, which was equivalent to the root mean square value in a practical application (Clancy et al. 2002). Knee extension for 15 s at each level was randomly added while maintaining constant plantar flexion torque (Fig. 1). The knee extension level was fed back to the subjects auditorily (not visually) because it was difficult for them to handle two visual feedbacks simultaneously. To obtain the brief ARV of the RF for the auditory feedback, the EMG of the RF was full-wave-rectified and low-pass-filtered at a cutoff frequency of 10 Hz online using LabChart software (ADInstruments, Sydney, Australia). During each trial, if this processed signal went beyond or fell below the range of the target level ± 10% of the corresponding value during the MVC (%MVC), the subjects received auditory feedback until the processed signal returned to the target range. At 100% KEMVC, the subjects were encouraged to perform maximum voluntary knee extensions, which were monitored by the processed signal. A few minutes of rest was allowed between trials at each plantar flexion level.

The data obtained in the main trials were processed as follows. The analysis program searched the 5-s window, where it obtained the minimum value of the absolute difference in the ARV of the RF between the target level and the produced value by moving the window through

the recorded time in 1/2000-s steps. The averaged torque and the ARVs of all muscles were calculated over the chosen window and were expressed as % MVC. These processes were completed using Matlab 2007a software (Mathworks, Natick, MA, USA).

Statistics

The statistical significances for the ARVs (expressed as % MVC) of the RF, MG, LG, and Sol were tested by two-way analysis of variance (ANOVA) with repeated measures (three plantar flexion levels × three knee extension levels). Shaffer's post-hoc test was conducted to examine the difference between the knee extension levels. If the interaction between the plantar flexion level and the knee extension level was significant, the post-hoc test included a multiple comparison for simple effects. The Greenhouse–Geisser degrees of freedom correction (ε) was used to correct for violation of the sphericity assumption. Eta-squared (η^2) and the power ($1-\beta$) were calculated to provide an indication of the adequacy of the sample size. The ANOVA, post-hoc test, and power test were performed with statistical software (SPSS 12.0J; SPSS Japan, Tokyo, Japan). The level of significance for all comparisons was set at $P < 0.05$.

Results

A typical example of the plantar flexion torque and the EMGs of all muscles during the 20% PFMVC trial is shown in Figure 2. The plantar flexion torque would be constant at all knee extension levels. Although the RF activity at 100% KEMVC seemed to fluctuate, the activation level was higher than that at 50% KEMVC. The MG showed tonic activation during isometric plantar flexion without knee extension, but its amplitude drastically decreased when isometric knee extension was added to the task. With MG activity depression, Sol activity was increased. LG activity did not show the modulation seen with MG activity. These observations were confirmed as follows.

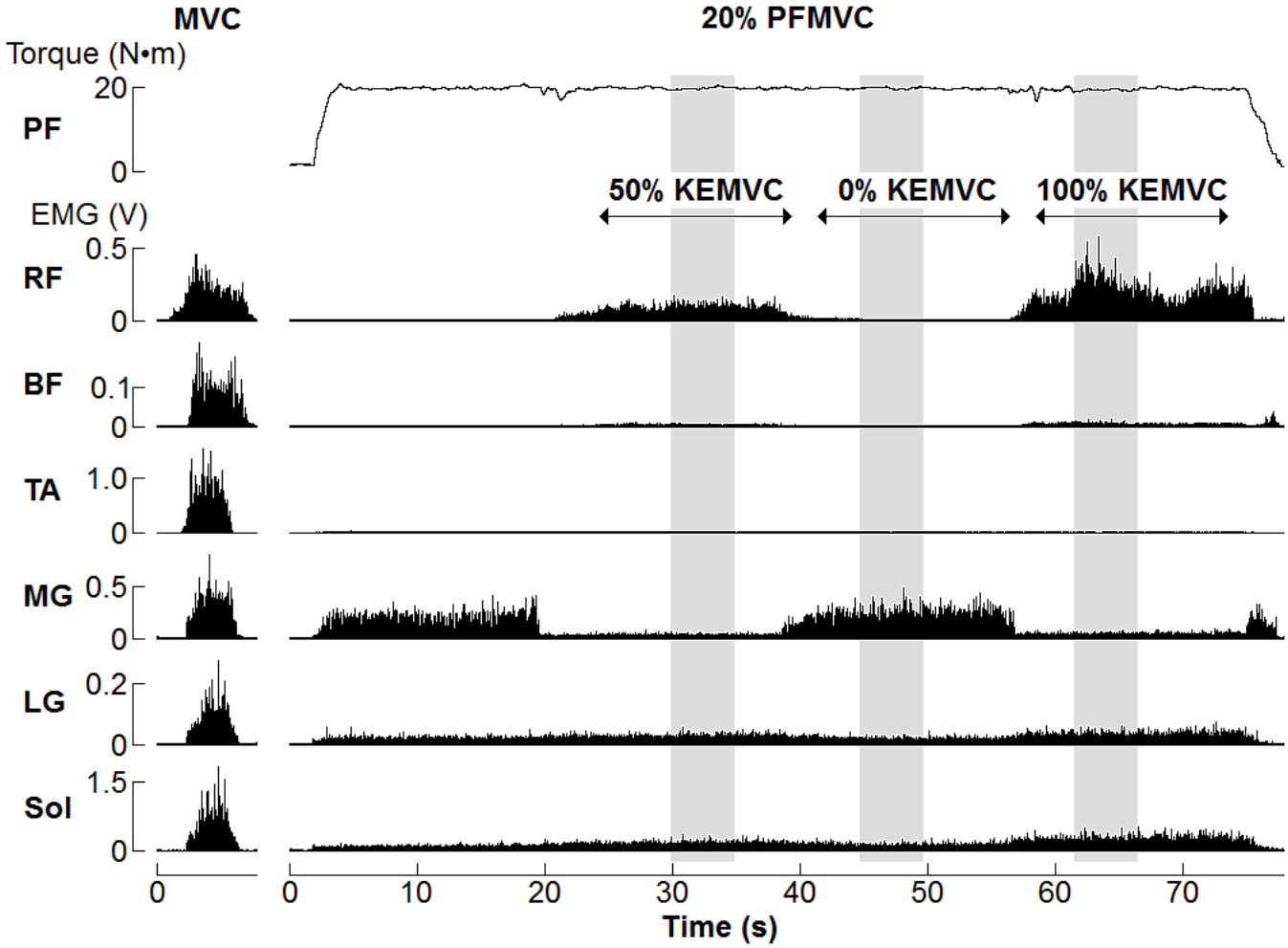

Fig. 2. Typical plantar flexion (PF) torque and electromyograms (EMGs). *Left*. Rectified EMGs during maximum voluntary contraction (MVC) trials for each muscle. *Right*. Torque and rectified EMGs during the 20% of plantar flexion MVC (%PFMVC) trial. EMGs were obtained from the rectus femoris (RF), biceps femoris (BF), tibial anterioris (TA), medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (Sol). Knee extension (KE) levels were set at 0% KEMVC (relaxation), 50% KEMVC, 0% KEMVC, and 100% KEMVC at 15-s intervals. Shaded areas represent the 5-s windows where the mean torque and average rectified values of EMG activities were calculated.

Table 1 shows group results of the controlled factors at all conditions. The errors between the target level and the produced torque were < 1% PFMVC under any of the conditions. At 50% and 100% KEMVC, the ARVs of the RF were about 40% and 80% MVC, respectively. Although they were somewhat lower than the target levels, the post-hoc test revealed that the ARV of the RF significantly increased with increasing knee extension level from 0% to 50%, from 50% to 100%, and from 0% to 100% KEMVC ($P < 0.001$ for each comparison). For all conditions, the ARVs of the BF and TA were < 10% and < 5% MVC, respectively.

Table 1. Plantar flexion torque and average rectified values for electromyographic activity of the controlled muscles under all conditions

%PFMVC	%KEMVC	%MVC			
		Torque	RF	BF	TA
10	0	10.0 (0.3)	2.7 (2.1)	2.0 (2.1)	3.1 (3.2)
	50	10.2 (0.2)	38.9 (6.6)	6.5 (2.8)	2.7 (3.1)
	100	10.2 (0.4)	72.2 (14.9)	9.1 (4.2)	4.2 (4.7)
20	0	20.1 (0.6)	2.6 (2.1)	2.6 (2.6)	3.7 (3.7)
	50	20.4 (0.6)	37.9 (7.5)	5.9 (2.6)	4.0 (3.8)
	100	20.5 (0.8)	74.0 (15.8)	9.0 (4.2)	3.2 (2.9)
30	0	29.9 (0.8)	2.5 (1.6)	3.2 (2.3)	3.4 (3.1)
	50	29.8 (0.9)	38.9 (7.0)	6.1 (3.2)	4.1 (3.3)
	100	30.7 (0.9)	74.8 (19.0)	9.6 (4.2)	3.9 (3.2)

MVC: maximum voluntary contraction; %PFMVC: target level of plantar flexion torque; %KEMVC: target level of average rectified value of electromyographic activity of rectus femoris; RF: rectus femoris; BF: biceps femoris; TA: tibial anterioris. The RF, BF, and TA were controlled in this study. The value in each cell is the mean (standard deviation). All values are represented as a percentage of the corresponding value during the MVC (%MVC).

The ARV of the MG significantly differed among the plantar flexion levels ($F_{2,18}$ = 18.5, ε = 0.953, η^2 = 0.24, 1-β = 0.99, P < 0.001) and among the knee extension levels ($F_{2,18}$ = 15.8, ε = 0.549, η^2 = 0.19, 1-β = 0.95, P = 0.002) (Fig. 3). The interaction between the plantar flexion level and the knee extension level was not significant ($F_{4,36}$ = 0.7, ε = 0.454, η^2 = 0.00, 1-β = 0.14, P = 0.502). Shaffer's post-hoc test revealed that the ARV of the MG significantly decreased with increasing knee extension level from 0% to 50% KEMVC (P = 0.002) and from 0% to 100% KEMVC (P = 0.005). There was no significant difference between 50% and 100% KEMVC (P = 0.529).

The ARV of the LG significantly differed among the plantar flexion levels ($F_{2,18}$ = 22.2, ε = 0.647, η^2 = 0.38, 1-β = 0.99, P < 0.001) but not among the knee extension levels ($F_{2,18}$ = 0.3, ε = 0.523, η^2 = 0.00, 1-β = 0.08, P = 0.596) (Fig. 3). The interaction was not significant ($F_{4,36}$ = 0.9, ε = 0.471, η^2 = 0.00, 1-β = 0.17, P = 0.415).

The ARV of the Sol significantly differed among the plantar flexion levels ($F_{2,18}$ = 68.9, ε = 0.674, η^2 = 0.39, 1-β = 1.00, P < 0.001) and among the knee extension levels ($F_{2,18}$ = 42.9,

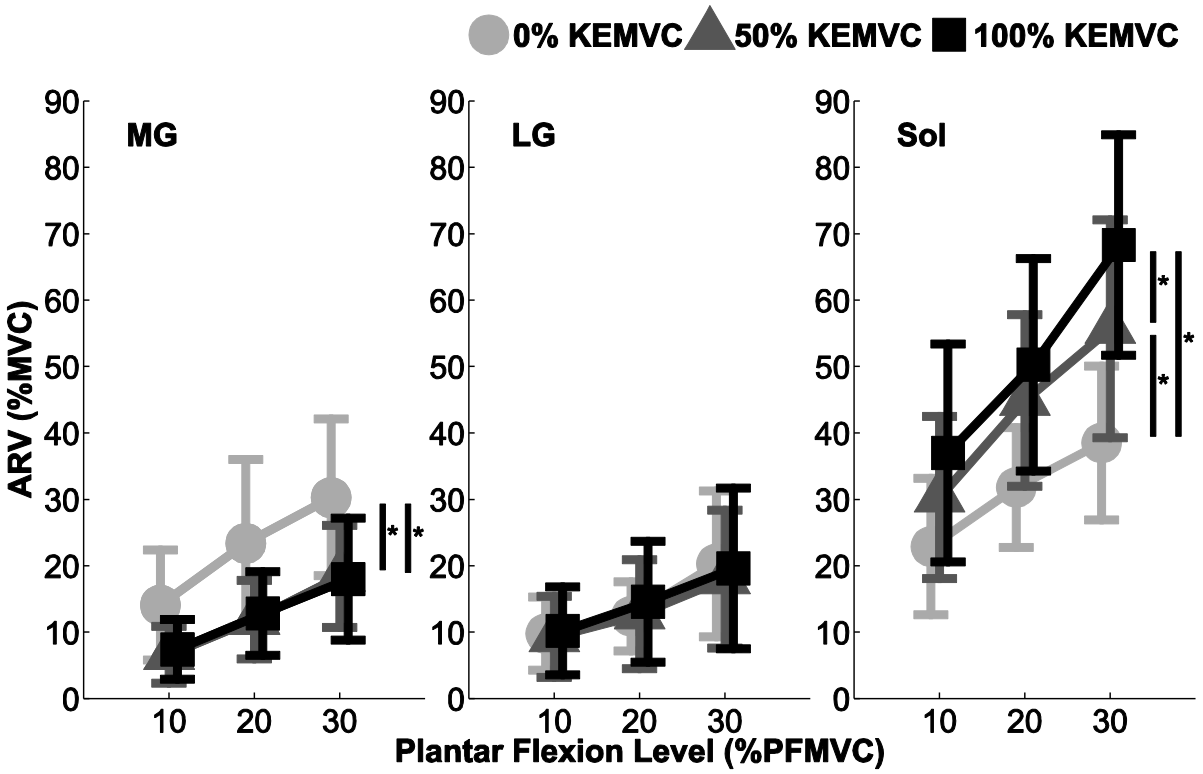

Fig. 3. Average rectified values (ARVs) of the electromyographic activity during the main trials at all combined conditions of the plantar flexion and knee extension levels. Error bars indicate the standard deviation. %KEMVC: target level of the rectus femoris ARV. Significant differences are indicated: $^{**}P < 0.01$; $^{***}P < 0.001$.

$\varepsilon = 0.740$, $\eta^2 = 0.30$, $1\text{-}\beta = 1.00$, $P < 0.001$) (Fig. 3). The interaction was not significant ($F_{4,36} = 2.8$, $\varepsilon = 0.473$, $\eta^2 = 0.03$, $1\text{-}\beta = 0.46$, $P = 0.091$). Shaffer's post-hoc test revealed that the ARV of the Sol significantly increased with increasing knee extension level from 0% to 50% KEMVC ($P < 0.001$), from 50% to 100% KEMVC ($P = 0.001$), and from 0% to 100% KEMVC ($P < 0.001$).

Discussion

Influence of knee extensor activation on the activities of plantar flexors

The main finding of the present study was that MG activity was depressed and Sol activity was increased when knee extension was added to plantar flexion. This finding suggests that knee extensor activity is related to selective activation of plantar flexor synergists.

Studies about voluntary single-joint movements suggested that knee extension with no

intended ankle motion were followed by unconscious activation of dorsiflexors (not plantar flexors), and conversely, dorsiflexion induced knee extensor activity (Aruin 2001; Dimitrijevic et al. 1992; Hwang and Abraham 2001). However, the results of the present study about voluntary multi-joint movements revealed not only the coupling of knee extensors and plantar flexors but also the differences in coupling patterns among plantar flexors. In this study, because the MG is a biarticular plantar flexor acting as an antagonist for knee extension, knee extensor activation resulted in reduced MG activity, which is seemingly in line with the concept of reciprocal inhibition, and increased activation of the Sol, which is a monoarticular plantar flexor. These results seem to be unique to multi-joint movements and depend on anatomical differences.

Selective activation among the synergists has been observed during sustained isometric plantar flexion without activation of knee extensors (McLean and Goudy 2004; Sirin and Patla 1987; Tamaki et al. 1998, 2011). For example, a previous study reported that Sol activity occasionally substituted other plantar flexors and increased to, at most, 30% MVC during 1 h of isometric plantar flexion at 10% PFMVC (McLean and Goudy 2004). In the present study, the ARV of the Sol increased to more than 30% MVC at 10% PFMVC concurrently with knee extension (Fig. 3). Especially at 30% PFMVC, the ARV of the Sol startlingly increased to 70% MVC with knee extension at 100% KEMVC (Fig. 3). These quantified amounts suggest that activation of knee extensors serves as a trigger to place a heavy load on the Sol.

Physiological mechanisms

The physiological mechanisms underlying the observed influence of knee extension on triceps surae activity may be explained by the activity at both the central and peripheral levels. The MG functions not only as a plantar flexor but also as a knee flexor. Thus, when voluntary knee extension is added to plantar flexion, the central drive for knee extension reduces MG activity because it works as an antagonist during knee extension. To compensate for the torque loss

induced by MG activity depression, the activation level of the Sol must increase. To this end, a greater central drive is provided to the Sol motoneuron pool. Additionally, the peripheral neural network from the quadriceps to the triceps surae would be related to the observed change in the triceps surae activation pattern. The reciprocal, or heteronymous, inhibition (Bayoumi and Ashby 1989; Hamm and Alexander 2010; Kudina 1980; Meunier et al. 1994) from the quadriceps could then inhibit knee flexor activity, including that of the MG.

There is another possible explanation—that increased Sol activity is followed by MG activity depression. A facilitatory heteronymous connection from the quadriceps to the Sol is so fundamental that it exists not only in human subjects, who have a number of transjoint neural pathways (Meunier et al. 1993), but also in certain animals, such as the cat and baboon, which have few transjoint neural pathways between the ankle and knee (Eccles et al. 1957; Hongo et al. 1984). For human movements requiring simultaneous motion of plantar flexion and knee extension, it has been reported that neural pathways from the quadriceps to the Sol are selected for task requirements (Barbeau et al. 2000; Kawashima et al. 2006; Lamy et al. 2008). For example, during the early stance phase of human walking, the stretch reflex from the quadriceps had a facilitatory effect on Sol activity (Kawashima et al. 2006), and heteronymous inhibition from the quadriceps to the Sol was reduced (Lamy et al. 2008). Partly because of selecting such facilitatory connections, quadriceps activation induces increased Sol activity. To maintain constant plantar flexion torque, MG activity would have to decrease with heteronymous inhibition from the Sol to the MG (Meunier et al. 1994).

As mentioned above, the peripheral neural pathways could provide a simple explanation for the observed selective activation. However, MG activity was not decreased with increasing knee extensor activation from 50% to 100% KEMVC. Although the inhibitory effect of knee extensor activation on MG activity would be saturated at low-intensity plantar flexion, Chapter II revealed that knee extensor activation at any levels had a facilitatory effect on MG

activity at high-intensity plantar flexion. To explain these phenomena through the peripheral neural pathways from the quadriceps muscles, various situation-dependent effects of these pathways are necessary. Alternatively, the muscle synergy hypothesis allows a better view that planar flexor activities are changed by recruited plantar flexor synergies depending on the presence of knee extensor activation. If the recruitment of plantar flexor synergies is determined by the presence of knee extensor activation as observed in Chapter II, it is understandable that MG activity is not drastically changed with increasing knee extensor activation from 50% to 100% KEMVC. Although the present study could not definitively identify which neural pathways to the MG and Sol are used during simultaneous motion of plantar flexion and knee extension, explanation based on muscle synergies is simpler and suitable for the observed selective activation.

Practical significance

The observed selective activation, wherein MG activity was depressed and Sol activity was increased during plantar flexion with simultaneous knee extension, allowed smooth straightening of the leg. Leg straightening—requiring simultaneous plantar flexion, knee extension, and hip extension—is a component of various daily and sporting activities, including jumping (Barbeau et al. 2000) and walking (Anderson and Pandy 2001; Franz and Kram 2012; Hof et al. 2005; Lamy et al. 2008). During leg straightening, MG activity would conflict with knee extensor activity because of its knee-flexing function. Conversely, the Sol is a monoarticular plantar flexor, so its activity directly increases push-off force. Some previous studies reported that MG activity was weaker than Sol activity at the early stance phase of walking, where knee extensors are strongly activated (Franz and Kram 2012; Hof et al. 2005). A simulation study also predicted coactivation of knee extensors and the Sol without MG activity at this phase (Anderson and Pandy 2001). Because of the anatomical difference, the Sol

is preferable to the MG for leg straightening.

The observed selective activation is consistent with the anatomical decision, but its practical significance in multi-joint movements could not be explained by anatomical function alone. Knee extensors could pull on the calcaneus as a result of the action of biarticular plantar flexors—so-called energy transfer (Bobbert et al. 1986; Prilutsky and Zatsiorsky 1994). If biarticular plantar flexors do not generate knee flexion torque, knee extensors could not act to accelerate the ankle to plantar flexion through these biarticular muscles, and the knee angle would reach the limit too early to perform the maximum mechanical work (van Ingen Schenau et al. 1987). Taking into account these mechanical characteristics of biarticular muscles, an adequate amount of MG activity is required in particular situations. Therefore, the anatomically reasonable activation may disturb the above-mentioned mechanical functions of the MG in some situations. Although the present study reveals selective activation depending on anatomical function, it is necessary to assess in which situation this phenomenon occurs and is effective.

Taking into consideration the physiological difference, there are effective situations, which is another significant practical aspect of this phenomenon. The MG is more easily fatigued than the Sol (Kawakami et al. 2000) because its ratio of type II fibers is three times that in the Sol (Johnson et al. 1973). It is possible that the observed substitution for muscle activation reduces the load on the MG, thereby delaying its exhaustion during prolonged multi-joint exercise, such as walking (Cronin et al. 2013), which requires plantar flexion and simultaneous knee extension. For example, during 1-h walking, the fascicle length at the ground contact and the range of its change through a stride decreased in the MG whereas those of the Sol were not significantly changed (Cronin et al. 2013). From the perspective of the force-length relationship, Sol activity would compensate for the loss of the force-generating capacity of the MG in a fatigue condition. This compensation would be facilitated by the observed substitution.

Moreover, a previous study reported that some knee extensor synergists alternated during sustained knee extension at 2.5% MVC for 1 h (Kouzaki and Shinohara 2006). The frequency of the alternation during muscle activity among the synergists negatively correlates with the amount of reduction in the MVC force (Kouzaki and Shinohara 2006). Although the generation mechanism underlying the substitution for muscle activation during a multi-joint movement should differ somewhat from that during a single-joint movement, it is possible that the observed substitutions among the plantar flexor synergists have a similar functional ability to reduce fatigue during a strenuous task. Therefore, knee extensor activation changes load sharing not only between the ankle and knee (Monaco et al. 2009) but also among plantar flexors, thereby potentially managing fatigue during a multi-joint exercise that requires leg straightening.

Limitations

There were two problems in the study regarding the physiological explanation of the attained results. First, although the MG and LG cross the ankle and knee and have almost the same muscle fiber composition (Johnson et al. 1973), LG activity was not depressed with knee extension—unlike MG activity (Figs. 1, 2). Earlier studies also reported that LG and MG activity occasionally had different responses to the same motion (Nardone and Schieppati 1988; Tamaki et al. 1998, 2011). For example, during eccentric isotonic plantar flexion against a 100-N load, the LG displayed high activation, whereas the MG showed little activity (Nardone and Schieppati 1988). Moreover, a previous study indicated the possibility that the MG and LG are differently controlled by neural pathways from the same origin (Duysens et al. 1996). The sural nerve stimulation had a facilitatory effect on the MG and an inhibitory effect on the LG during the middle and late stance phase of walking (Duysens et al. 1996). Therefore, LG activity could be regulated separately from the MG for the task used in the study although the characteristics of neural circuits from the quadriceps have been unclear.

Second, the change in the ARV of the MG was not always proportional to that of the Sol. For example, increasing the knee extension level from 50% to 100% KEMVC resulted in the ARV of the MG remaining at almost the same level, whereas that of the Sol significantly increased (Fig. 3). The physiological cross-sectional area (PCSA), the total cross-sectional area of all of the muscle fibers at right angles to their long axes, is known to be a good predictor of the generation capacity of muscle force (Fukunaga et al. 2001). The Sol has a larger PCSA than the MG (Friederich and Richard 1990). Taking into consideration the difference in the PCSA between these muscles, the estimated torque increase induced by the increased Sol activity was larger than the decrease in the plantar flexion torque induced by MG activity depression. However, the MG has a three times higher ratio of type II fibers than the Sol (Johnson et al. 1973), and type II fibers generate more force than type I fibers. The difference in muscle fiber composition reduces the estimated torque increase by the Sol.

In another aspect, recent studies reported that muscle activities were different in several portions of a single muscle, such as the MG and RF. Additionally, the surface EMG technique recorded muscle activity only at the relatively narrow area underneath the electrode (Hodson-Tole et al. 2013; Watanabe et al. 2012). For example, recorded EMG activity was different at each electrode in the MG, and the distal portion of the MG was mainly activated during standing (Hodson-Tole et al. 2013). Although the depression of MG activity detected was small in this study, there was the potential for a greater decrease in muscle activity in other portions of the MG. Additionally, other small plantar flexors (e.g., peroneus brevis, posterior tibialis) contribute at least 20% of the plantar flexion torque (Murray et al. 1976). Because there is an inhibitory pathway from the quadriceps to the peroneus brevis (Meunier et al. 1994), it is possible that simultaneous knee extensor activation causes the activity of such small muscles to decrease. (The activities of these muscles can barely be measured by surface EMG.) When we take into consideration the combined decreased activation of the MG, the activity spatial

difference within the MG, and the small plantar flexors, the torque increase by the Sol was not excessive.

Conclusions

The present study revealed that when knee extensor activity is added to plantar flexion MG activity is depressed and Sol activity is increased. The quantified amounts of change indicate that knee extensor activation has an important influence on load sharing among plantar flexors. The results suggest that monoarticular plantar flexors (not biarticular plantar flexors, which also function as knee flexors) are selectively activated depending on the preference of their anatomical characteristics for simultaneous knee extension.

Section II of Chapter III

Plantar flexor activities depend on muscle synergies with varying in task-irrelevant subspace

Introduction

During a human movement, the central nervous system converts the uncertain biological mechanics into robust motor behaviors. Various neural and mechanical noises cause trial-to-trial variability (Faisal et al. 2008), resulting in long-range changes according to complex muscle mechanics that include muscle fiber length, muscle contraction velocity, and so on (Cheng et al. 2000). If all these factors are corrected for the desired state (Adams 1971), the central nervous system should handle all feedback information about the states of the above-mentioned factors. However, because the large degrees of freedom in human movements enable the central nervous system to achieve the task goal even in undesired ways (Bernstein 1967), it would be better to select the important information for a given task.

Because control of the task-irrelevant variability is unproductive, the uncontrolled manifold hypothesis has proposed that the variability that influence the task performance is corrected but the other variability is left (Scholz and Schöner 1999; Schöner 1995). From a slightly different perspective, the optimal feedback control hypothesis has insisted that feedback information of the task-relevant variability is selectively used for correcting the movement with reducing focused information and maintaining the performance (Todorov and Jordan 2002). Many studies in this field have evaluated the kinetics at a task of force production of fingers of a hand (Scholz et al. 2002) and the joint kinematics at reaching tasks, such as the sit-to-stand movement (Scholz and Schöner 1999), bimanual motor task (Diedrichsen 2007), and pistol shooting (Scholz et al. 2000).

Recently, the uncontrolled manifold approach was applied to muscle activation, and it

was reported that the variability of index finger muscle activities that affected the fingertip force was smaller than their task-irrelevant variability (Valero-Cuevas et al. 2009). One interpretation (Tresch and Jarc 2009) is that this small variability suggested that each muscle was independently controlled and activity that did not affect the task (i.e., the fingertip force) was uncontrolled. This interpretation emphasizes the independent control of muscle activities and seemingly contradicts the hypothesis that muscle synergies neurally constrained muscle activities (Tresch et al. 1999). To integrate these contradictory hypotheses, it is necessary to investigate whether the task-irrelevant variability is randomly sparse in all task-irrelevant subspaces or has a structure that suggests a muscle synergy. Chapter II revealed that plantar flexor activities at a large scale has at least two structure that suggest the existence of muscle synergies. Therefore, close observation of the variability of plantar flexor activities during low-intensity plantar flexion with or without knee extension would resolve the discrepancy between the uncontrolled manifold hypothesis at the muscle activation level and the muscle synergy hypothesis.

We hypothesized that plantar flexor activities fluctuate in muscle synergy subspaces, which overlap with the torque-irrelevant subspaces. To test this hypothesis, we investigated the variability of plantar flexor activities during voluntary isometric plantar flexion performed with or without voluntary isometric knee extension.

Methods

Subjects

Six male volunteers participated in the experiment. The mean ± standard deviation age, height, and body mass of the subjects was 22.3 ± 1.7 years, 176.0 ± 3.4 cm, and 68.5 ± 7.1 kg, respectively. No subject had any significant medical history or any signs of a neurological disorder. All subjects gave their written informed consent to participate in the study after

receiving a detailed explanation of the purposes, potential benefits, and risks associated with participation. The Human Research Ethics Committee at Kanagawa University approved all procedures used in the study.

Torque and electromyography (EMG) recordings

For all trials, the subject lay prone on a flat seat and the legs were secured with straps placed around the waist, knees and right ankle to minimize changes in joint angles. The knees were fully extended and were supported by pads that elevated the knee to prevent contact between the seat and the electrodes placed over the vastus lateralis (VL) and rectus femoris (RF) muscles. The right ankle was positioned at 0° (neutral) and the right foot was tightly fixed to the plate of a dynamometer (Biodex System 4, Biodex Medical Systems, Shirley, NY, USA). The axis of rotation of the dynamometer was aligned with the anatomical axis of ankle dorsiflexion and plantar flexion. Special care was taken to ensure that the ankle and knee angles were constant throughout the experiment to remove any influence of joint angle on the electromyographic (EMG) activity of plantar flexor muscles (Cresswell et al. 1995).

Surface EMG was recorded from the VL, RF, gluteus maximus (GM), biceps femoris (BF), tibialis anterior (TA), peroneus longus (PL), peroneus brevis (PB), medial gastrocnemius (MG), lateral gastrocnemius (LG), and soleus (Sol) muscles of the right leg using single differential electrodes (DE-2.1, Delsys, Boston, MA, USA). After carefully abrading and cleaning the skin with alcohol, the electrodes were placed according to the SENIAM recommendation (Freriks et al. 1999), and the ground electrode was placed on the tuberositas tibiae. The EMG signals were amplified (×100) using a standard biosignal recording system (Bagnoli Desktop, and Handheld EMG Systems, Delsys), and bandpass filtered at 20–450 Hz before sampling. Plantar flexion torque and EMG data were sampled at 2 kHz on the hard disk of a personal computer using a 16-bit analog-to-digital converter (PowerLab 16/35, AD

Instruments, Sydney, Australia).

Experimental protocol

The experimental session consisted of maximal voluntary isometric contraction (MVC) trials followed by torque-matching trials in which the subject was required to generate a constant isometric plantar flexion torque while changing a level of isometric knee extensor activation. Isometric plantar flexion with changing isometric knee extensor contraction levels could lead to various activation patterns of plantar flexor muscles with maintaining only one mechanical constraint.

Before the experiment, subjects practiced until they could generate the torque as intended. At the beginning of the session, subjects performed MVC trials for hip extension, knee flexion, knee extension, ankle dorsiflexion, ankle eversion, and ankle plantar flexion. The level of effort was gradually increased to a maximum to avoid an EMG burst at the start of the contraction. Verbal encouragement was provided for each MVC trial. Each MVC trial lasted >3 s. Two trials were performed for each muscle group. A rest period of >1 min was provided between consecutive MVC trials. EMG was recorded during all MVC trials, but torque was measured only for the plantar flexion MVC trials. The maximum torque generated during the plantar flexor MVC trials (PFMVC) and the maximum average rectified value (ARV) of the VL EMG during the knee extensor MVC trials (KEMVC) were identified.

After a rest period of >1 min, subjects performed the torque-matching trials. They performed constant isometric plantar flexion at 10, 20, and 30% of the PFMVC (%PFMVC) in random order. They performed each plantar flexion once at each level. They were asked to set the plantar flexion torque as close as possible to the target level during the first 15 s. After the first 15 s, they were asked to add knee extensor activation to the plantar flexion. The knee extensor activation levels were set at 0, 50, and 100% of the maximum voluntary isometric knee

extensor activation (%KEMVC). Knee extensor contraction for 15 s at each level was randomly added while maintaining constant plantar flexion torque. The subjects were then asked to press a plate in the same manner for all knee extension conditions. A rest period of >1 min was allowed between consecutive trials. The plantar flexion torque, target plantar flexion torque, minimally processed VL EMG, and target VL EMG were displayed in real time on a 22-inch monitor (AL2216W, Acer, New Taipei, Taiwan) located in front of the subject. The minimally processed EMG used for feedback purposes was full-wave rectified and averaged every 250 ms using LabChart software (AD Instruments). Subjects were also provided with auditory feedback of the level of knee extensor activity, because it was difficult for them to simultaneously process two forms of visual feedback. If the minimally processed VL EMG was above or below the target KEMVC by ≥10% KEMVC, the subjects received auditory feedback until the processed signal returned to the target range. At 100% KEMVC, the subjects were encouraged to perform a maximal voluntary knee extension.

Data processing

Post processing of the data was performed using in-house MATLAB algorithms (version 2014b, MathWorks, Natick, MA, USA). For the MVC trials, a 1-s analysis window was moved through the recorded data in 1/2000-s steps. For the ankle plantar flexion MVC trials, torque was averaged over each window. PFMVC torque was defined as the largest of the mean values obtained from all windows over the two trials. The MVC of MG, LG, and Sol was calculated as the ARV in the window in which PFMVC occurred. This analysis depended on the widespread definition that the EMG during the MVC corresponded to the MVC torque in the same moment (Disselhorst-Klug et al. 2009). For the MVC trials for hip extension, knee flexion, knee extension, ankle eversion, and ankle dorsiflexion, a 1-s analysis window was moved through the recorded data in 1/2000-s steps and the ARV was calculated over each 1-s window.

Because the torque was not measured during the hip extension, knee flexion, knee extension, ankle eversion, and ankle dorsiflexion MVC trials, the ARVs of the GM, BF, VL, RF, TA, PL, and PB during MVCs were determined as the largest of the ARVs obtained from all windows over the two MVC trials for each muscle.

For the torque-matching trials, the analysis program searched the 15-s window, where it obtained the minimum absolute difference in the ARV of the VL between the target level and the produced value by moving the window through the recorded time in 1/2000-s steps. Within the chosen window, the average plantar flexion torque and the ARV were calculated every 1 s and expressed as a percentage of the corresponding value during MVC (%MVC).

Prediction of plantar flexion torque given EMG

The average plantar flexion torque and the ARVs of all muscles were calculated at 135 data points because three plantar flexion torque levels and three knee extensor activation levels were conducted and the ARVs were calculated every 1 s (i.e., 15 data points). To avoid over-fitting, the ARVs of plantar and dorsiflexors (i.e., six muscles) at each 5 s (27 data points; i.e., 20% of all data points) were combined into a 6 × 27 matrix ($EMG_{o\ ank}$), where the numbers of the row and column indicate the numbers of plantar and dorsiflexor muscles and data points, respectively, and this matrix and a average torque vector (t) at the same data points were used for calculating the model parameter. The prediction of plantar flexion torque made by given ARVs was based on the linear model: $t \approx c\ EMG_{o\ ank}$, where c is a model parameter vector (1 × 6). Because c maps the ARVs into exerted plantar flexion torques, c represents the task-relevant subspace.

Non-negative matrix factorization (NMF)

The ARVs at the same data points for calculating the linear model parameter (i.e., 27 data

points) were used for the NMF (Lee and Seung 2001). The ARVs of all muscles were combined into a 10 × 27 matrix (EMG_o), where the numbers of the row and column indicate the number of muscles and data points, respectively. For each subject, the NMF algorithm was applied to EMG_o. Because at least three synergies were necessary to explain plantar flexor activities at the low plantar flexion torque (see Chapter II), the number of synergies was set as three. The NMF found the properties of the synergies by populating two matrices: an 8 × 3 matrix (W), which specified the relative weighting of muscles in each synergy, and a 3 × 27 matrix (H), which specified the recruitment of each synergy in each condition. When these two matrices were multiplied, a 10 × 27 matrix (EMG_r) was created to reconstruct EMG_o: $EMG_r = W H$ (cf., $EMG_o \approx W H$). Within this framework, the NMF performed an iterative optimization from various random initial values until it converged on two matrices that minimized the sum of the squared errors: $\sum(EMG_o - EMG_r)^2$. To provide an indication of the adequacy of the number of synergies, the variability accounted for (Torres-Oviedo et al. 2006) was calculated as the ratio of the sum of the squared EMG_r to the sum of the squared EMG_o: variability accounted for (%) = $100 \times (\sum EMG_r^2 / \sum EMG_o^2)$.

For each subject, the recruitments (r; 1 × 27) in the situation that only one synergy vector reconstructed $EMG_{o\ ank}$ was calculated using each weighting vector of plantar and dorsiflexor muscles (w_{ank}; 6 × 1) in W: $r \approx w_{ank}^{+}\ EMG_{o\ ank}$, where w_{ank}^{+} (1 × 6) is a pseudo inverse of w_{ank}. Such equations were written for all three synergy weighting vectors. Because w_{ank}^{+} maps the ARVs into the recruitments of each synergy, w_{ank}^{+} represents the subspace relevant to each synergy.

The local synergies for each subject were clustered into global synergies for all subjects. For each subject, each local synergy was clustered into a different global synergy. The relative weighting of each muscle in each global synergy was the average relative weighting of that muscle in all local synergies contained within that global synergy. Adequate clustering was

determined as the clustering that minimized the sum of the squared distance between the recruitment of the global synergy and that of the local synergy clustered into it. The genetic algorithm combined with simulated annealing (Tsoi et al. 1995) was applied to identify adequate clustering. Then, the adequate global synergy set was calculated for this clustering. The recruitment of the global synergy in each condition was the recruitment of local synergies clustered into it.

Projection of ARV variance onto task-relevant, task-irrelevant, and synergy-relevant subspaces

The ARVs of plantar and dorsiflexor muslces that were not used for subspace calculation were combined into a 6 × 108 matrix ($EMG_{o\ ank\ remained}$), similar to $EMG_{o\ ank}$. The projected variance of the ARVs per dimension was compared across the task-relevant subspace (i.e., c), task-irrelevant subspace (i.e., nullspace of c), and synergy-relevant subspace (i.e., w_{ank}^{+}). The projected variance was calculated by the formula: $u\ V_{emg}\ u^{T}$, where V_{emg} is a covariance matrix of $EMG_{o\ ank\ remained}$ and u is a unit vector of each subspace (i.e., c and w_{ank}^{+}, and their norms are normalized to one). For the variance in the task-irrelevant subspace, the variance in the task-relevant subspace was subtracted from the full variance (i.e., the sum of the diagonal components of V_{emg}). This variance was averaged over the number of axes of the nullspace (Scholz and Schöner 1999; Valero-Cuevas et al. 2009). In this study, the dimension of the nullspace was five because the dimensions of $EMG_{o\ ank\ remained}$ and the task-relevant subspace were six and one, respectively. Because the most recruited synergy (i.e., the synergy vector closest to the resultant ARVs) was changed for each condition, the variance in the synergy-relevant subspace for each condition was defined as the largest variance in three synergy subspaces for each subject. Each variance per dimension in the task-relevant, task-irrelevant, and synergy-relevant subspaces was expressed as a percentage of the full variance.

Projection of the variance of the synergy recruitment onto task-relevant and task-irrelevant subspaces

The recruitments of muscles synergies ($H_{remained}$; 3 × 108) for $EMG_{o\ ank\ remained}$ using the weightings of plantar and dorsiflexor muscles in W (W_{ank}; 6 × 3) were calculated by the following formula: $H_{remained} = W_{ank}^{+}\ EMG_{o\ ank\ remained}$, where W_{ank}^{+} is a Moore-Penrose pseudo inverse matrix of W_{ank}. Because plantar flexion torques and $EMG_{o\ ank\ remained}$ could be connected by $t \approx c\ EMG_{o\ ank\ remained}$, plantar flexion torques was predicted by $H_{remained}$ using the following formula: $t \approx c_h\ H_{remained}$, where c_h is a matrix product (1 × 3) of c and W_{ank}. Because c_h maps the recruitments of muscle synergies into exerted plantar flexion torques, c_h represents the task-relevant subspace.

The projected variance of the synergy recruitments per dimension was compared across the task-relevant subspace (i.e., c_h) and task-irrelevant subspace (i.e., nullspace of c_h). The projected variance was calculated by the formula: $c_h\ V_h\ c_h^T$, where V_h is a covariance matrix of $H_{remained}$ and the norm of c_h is normalized to one. For the variance in the task-irrelevant subspace, the variance in the task-relevant subspace was subtracted from the full variance (i.e., the sum of the diagonal components of V_h). This variance was averaged over the number of axes of the nullspace (i.e., two). Each variance per dimension in the task-relevant and task-irrelevant subspaces was expressed as a percentage of the full variance.

Statistics

For the ARVs of plantar and dorsiflexor muscles, the projected variances per dimension were compared across the subspaces (task-relevant, task-irrelevant, and synergy-relevant subspace), plantar flexion torques (10, 20, and 30% PFMVC) and knee extensor activation levels (0, 50, and 100% KEMVC) using a three-way analysis of variance with repeated measures. For the synergy recruitments, the projected variances per dimension were compared across the

subspaces (task-relevant and task-irrelevant subspace), plantar flexion torques (10, 20, and 30% PFMVC) and knee extensor activation levels (0, 50, and 100% KEMVC) using a three-way analysis of variance with repeated measures. Shaffer's post-hoc test for a main effect was conducted to examine the difference between the subspaces. If the interaction was significant, post-hoc tests included a multiple comparison for simple effects. The Greenhouse-Geisser degrees of freedom correction (ε) was used to correct for violation of the sphericity assumption. The analysis of variance and post-hoc tests were performed with statistical software (SPSS Statistics 21, IBM Japan, Tokyo, Japan). The level of significance for all comparisons was set at $P < 0.05$.

Results

Variance of the ARVs in each subspace

Figure 1 shows the weightings of each synergy extracted by the NMF. *Synergy A* had the large weightings of all plantar flexor muscles while *Synergy B* mainly had the weightings of monoarticular plantar flexor muscles. *Synergy C* had both large weightings of knee extensor muscles and small weightings of monoarticular plantar flexor muscles. Because the variability accounted for was 98.4 ± 0.5 %, the preset number of synergies (i.e., three) was enough, based on the standard criterion that the variability accounted for was >90% (Torres-Oviedo et al. 2006). The assigned three synergies were used in the following analyses.

A typical scatter plot of MG and PL ARV across the different plantar flexion torques and knee extensor activation levels is shown in Figure 2. Although this figure only shows one of the plane extracted from six dimension for clarity, we can see that the ARVs were widely scattered in the task-irrelevant subspace (the left panel of Fig. 2). During plantar flexion alone, the ARVs lie on the line of the subspace relevant to *Synergy A*, and with adding knee extensor activation, they move toward the line of *Synergy B* (the right panel of Fig. 2). These observed

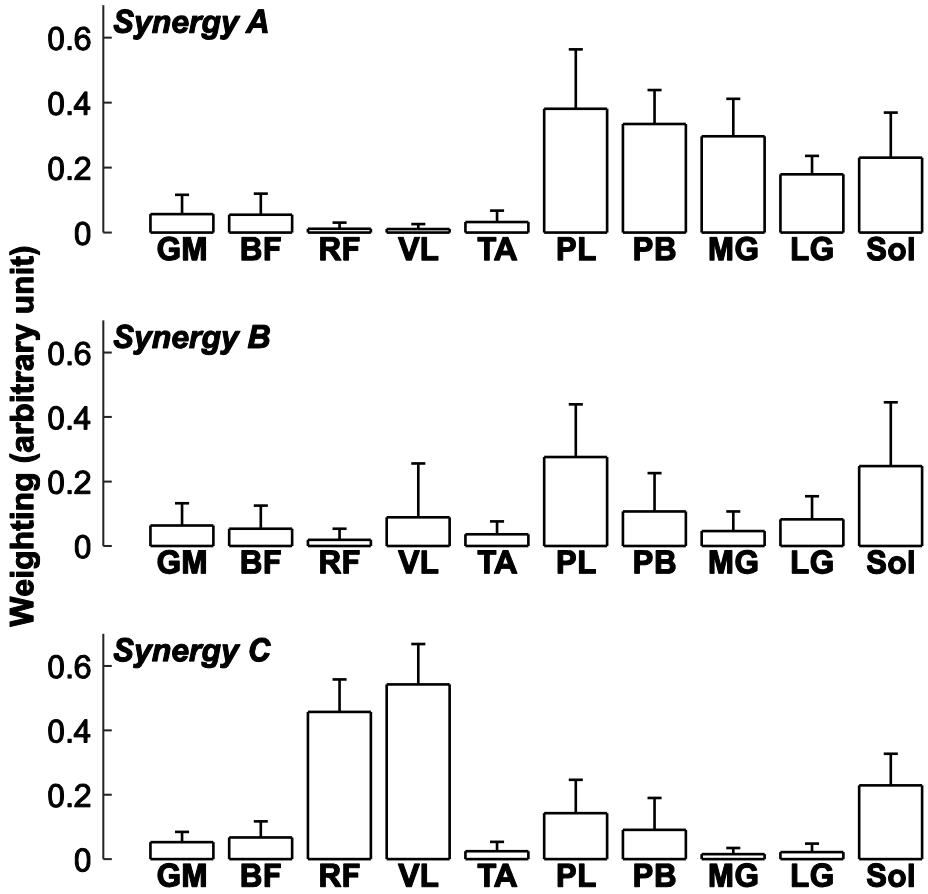

Fig. 1. Global synergy set. The average rectified values of the electromyographic activity of all muscles for each subject were decomposed into a synergy-weighting matrix and a recruitment matrix using non-negative matrix factorization. Each global synergy is the mean weighting of all subjects' synergies clustered into it. The error bars indicate standard deviation. GM: gluteus maximus; BF: biceps femoris; RF: rectus femoris; VL: vastus lateralis; TA: tibialis anterior; PL: peroneus longus; PB: peroneus brevis; MG: medial gastrocnemius; LG: lateral gastrocnemius; Sol: soleus.

ARVs would not randomly spread but seem to have more than one structure. These observations were confirmed in the subsequent analysis.

For the variance of the ARVs of plantar and dorsiflexor muscles, there was a significant main effect of subspace ($F_{2,10}$ = 19.4, ε = 0.702, P = 0.002) but no effect of plantar flexion torque ($F_{2,10}$ = 2.9, ε = 0.694, P = 0.132) and knee extensor activation ($F_{2,10}$ = 1.6, ε = 0.758, P = 0.262; Fig. 3). There was no significant interaction between subspace and plantar flexion torque ($F_{4,20}$ = 2.8, ε = 0.445, P = 0.118), between subspace and knee extensor activation ($F_{4,20}$ = 0.7, ε = 0.368, P = 0.487), between plantar flexion torque and knee extensor activation ($F_{4,20}$ = 0.9, ε = 0.685, P = 0.446), and between subspace, plantar flexion torque, and knee extensor

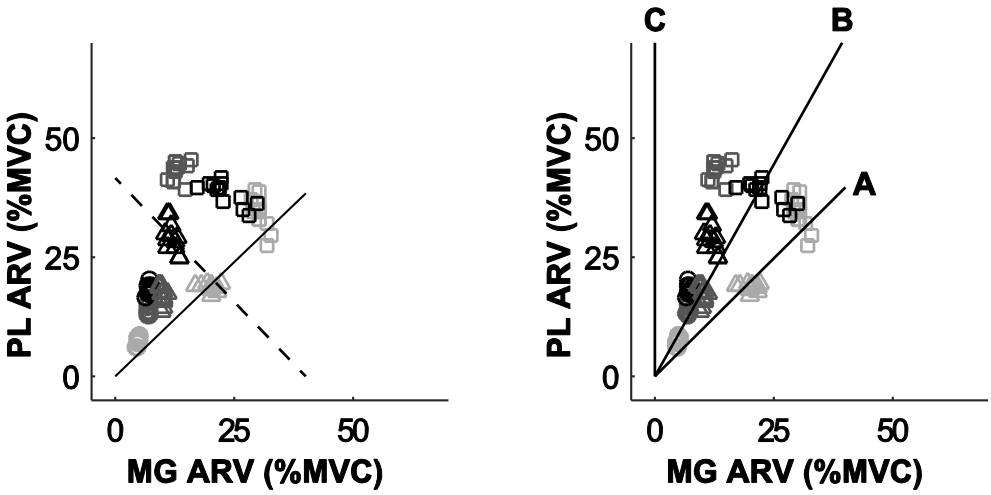

Fig. 2. Example scatter plot of the average rectified value (ARV) of the electromyographic (EMG) activity of the medial gastrocnemius (MG) and peroneus longus (PL) at different plantar flexion torques. In the left panel, the solid line and the dashed line represented the task-relevant subspace and the task-irrelevant subspace, respectively. In the right panel, the solid lines assigned A, B, and C represented the subspace relevant to *Synergy A*, *B* and *C*, respectively. The ARV of the EMG expressed as a percentage of the corresponding value during maximal voluntary contraction (%MVC). The subjects performed constant isometric plantar flexion at 10% (circles), 20 (triangles), and 30% (squares) of the maximum plantar flexion torque. They were asked to add knee extensor activation to the plantar flexion. The knee extensor activation levels were set at 0% maximum (light grey), 50% maximum (dark grey), and 100% maximum (black).

activation ($F_{8,40}$ = 1.1, ε = 0.387, P = 0.379). Shaffer's multiple comparison test for a main effect revealed that the variance in the synergy-relevant subspace was significantly larger than those in the task-relevant and task-irrelevant subspaces (P = 0.003 and P = 0.017, respectively), and the variance in the task-irrelevant subspace was significantly larger than that in the task-relevant subspace (P = 0.015).

The variance of the ARVs in the subspace relevant to *Synergy C*, which had the weightings of knee extensor and plantar flexor muscles (Fig. 1), was always smaller than those in the subspace relevant to the other synergies. Therefore, the variance in the subspace relevant to *Synergy C* was not involved in the above-mentioned variances in the synergy-relevant subspace. Because the weightings of *Synergy C* represented a simple linear interaction from knee extensor muscles to plantar flexor muscles, the small variance in the subspace relevant to *Synergy C* indicated that this simple interaction could not explain a drastic change in plantar

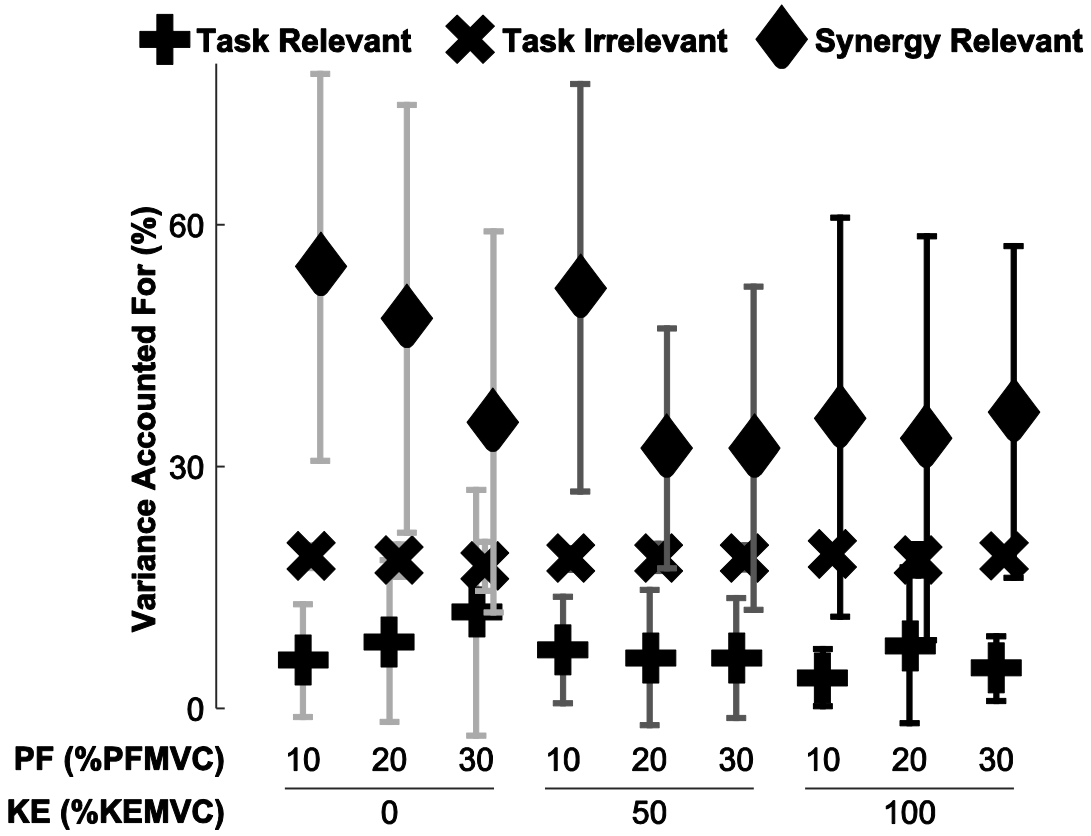

Fig. 3. The variance in the task-relevant (+), task-irrelevant (×), and synergy-relevant subspaces (♦). The data points indicate the mean, and the error bars indicate the standard deviation. The subjects performed constant isometric plantar flexion at 10, 20, and 30% of the maximum plantar flexion torque. They were asked to add knee extensor activation to the plantar flexion. The knee extensor activation levels were set at 0% maximum (light grey), 50% maximum (dark grey), and 100% maximum (black). Significant differences for main effects are indicated among the subspaces: * $P < 0.05$.

flexor activities induced by knee extensor activation.

Variance of the synergy recruitments in each subspace

Figure 4 shows the recruitment patterns of muscle synergies at all conditions. In the upper left panel, the recruitments of all muscle synergies are shown, and they are sorted into knee extensor activation levels in the other panels. Especially at 0% KEMVC, the recruitments of *Synergy A* and *B* are clearly scattered in the task-irrelevant subspace (the upper right panel of Fig. 4). Although the task-irrelevant subspace includes the axis of *Synergy C*, the dependence of synergy recruitments on the task-irrelevant subspace is observed on the plane of *Synergy A* and *B*, even

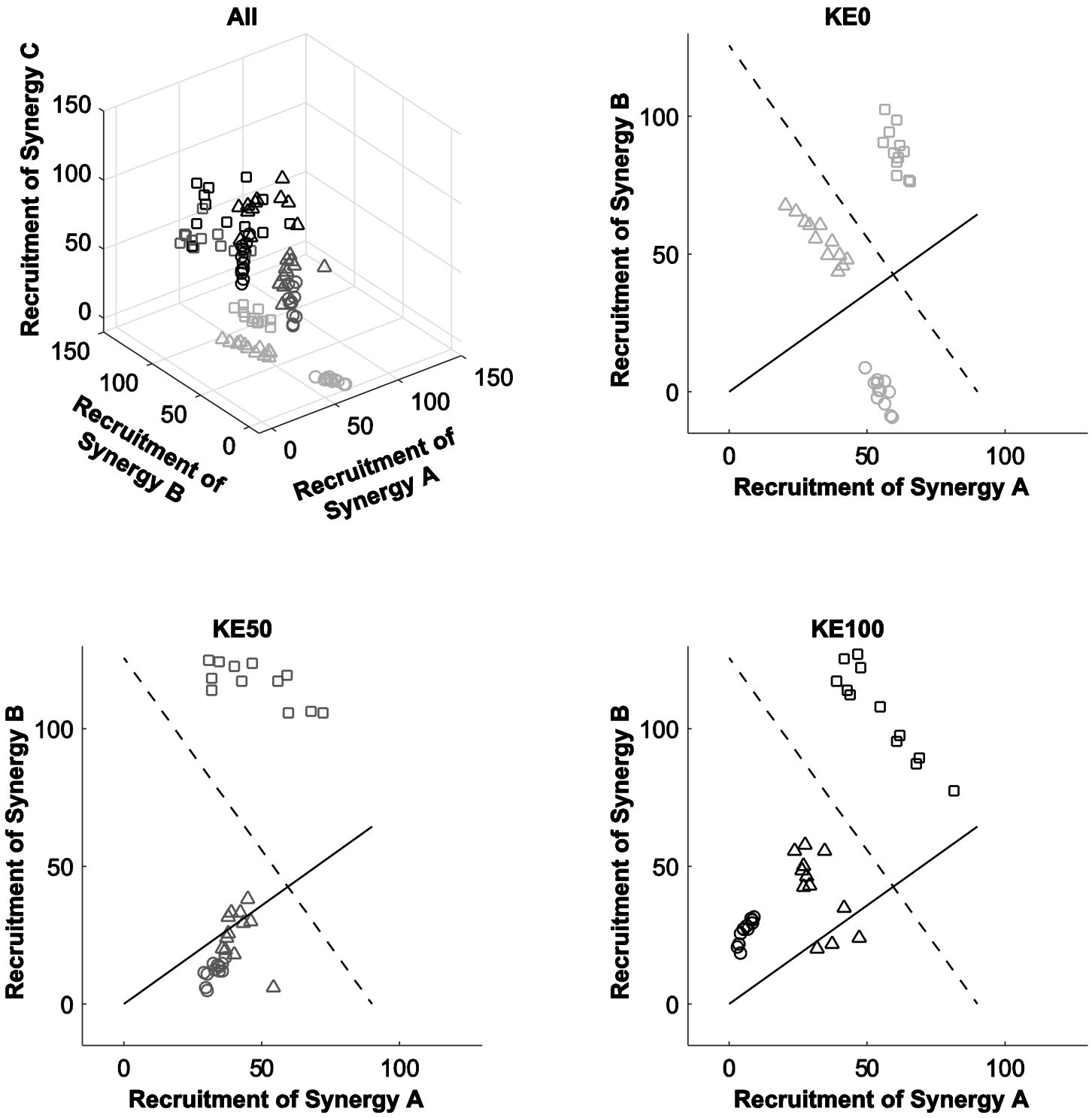

Fig. 4. Example scatter plot of the synergy recruitment at all conditions. Except for the upper left panel, the solid line and the dashed line represented the task-relevant subspace and the task-irrelevant subspace, respectively. The recruitment of muscle synergies is expressed in arbitrary units. The subjects performed constant isometric plantar flexion at 10% (circles), 20 (triangles), and 30% (squares) of the maximum plantar flexion torque. They were asked to add knee extensor activation to the plantar flexion. The knee extensor activation levels were set at 0% maximum (KE0; light grey), 50% maximum (KE50; dark grey), and 100% maximum (KE100; black).

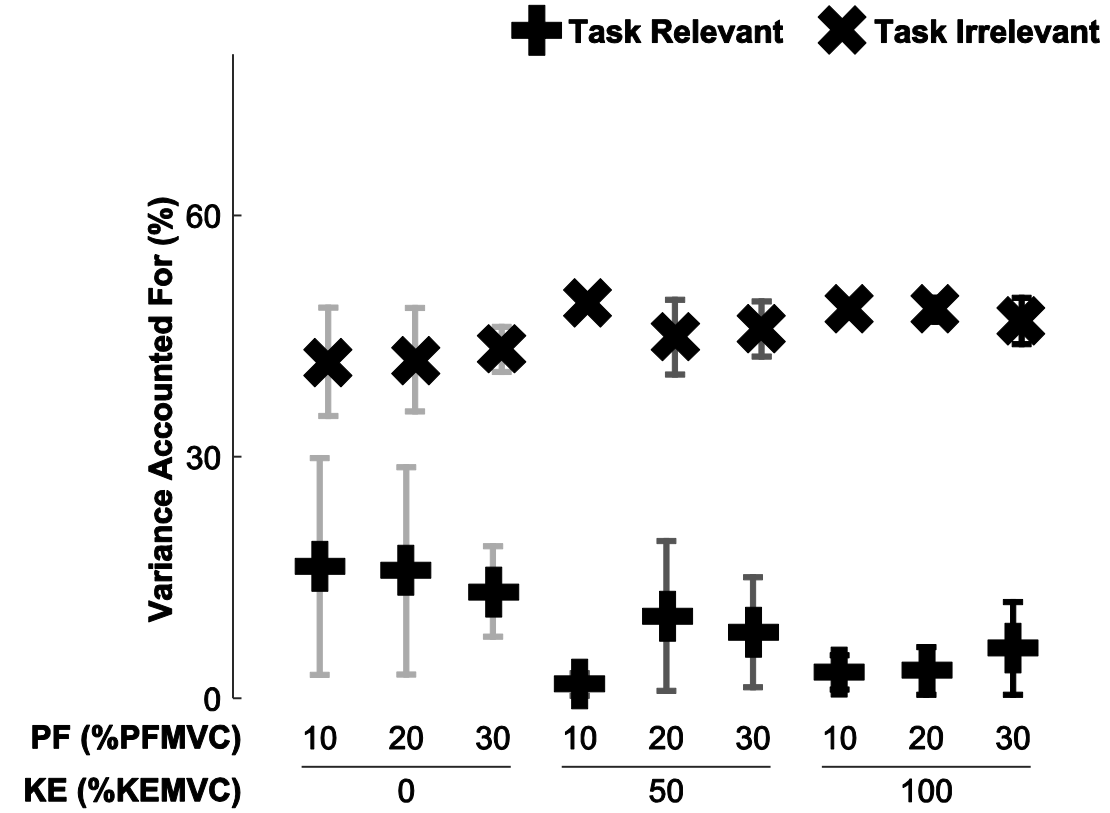

Fig. 5. The variance in the task-relevant (+) and task-irrelevant subspaces (×). The data points indicate the mean, and the error bars indicate the standard deviation. The subjects performed constant isometric plantar flexion at 10, 20, and 30% of the maximum plantar flexion torque. They were asked to add knee extensor activation to the plantar flexion. The knee extensor activation levels were set at 0% maximum (light grey), 50% maximum (dark grey), and 100% maximum (black).

at knee extension conditions, which change the recruitment patterns at the axis of *Synergy C* (the lower panels of Fig. 4). These observations were confirmed in the subsequent analysis.

For the variance of muscle synergy recruitments, there was a significant main effect of subspace ($F_{1,5}$ = 350.6, ε = 1.000, P < 0.001) but no effect of plantar flexion torque ($F_{2,10}$ = 0.6, ε = 0.881, P = 0.540) and knee extensor activation ($F_{2,10}$ = 5.4, ε = 0.740, P = 0.042; Fig. 4). There was a significant interaction between subspace and knee extensor activation ($F_{2,10}$ = 5.4, ε = 0.739, P = 0.043), but no significant interaction between subspace and plantar flexion torque ($F_{2,10}$ = 0.6, ε = 0.887, P = 0.528), between plantar flexion torque and knee extensor activation ($F_{4,20}$ = 1.7, ε = 0.610, P = 0.226), and between subspace, plantar flexion torque, and knee extensor activation ($F_{4,20}$ = 1.7, ε = 0.610, P = 0.227). Shaffer's multiple comparison test for a simple effect revealed that the variance of the synergy recruitments in the task-irrelevant

subspace was significantly larger than that in the task-relevant subspace at all nine (three plantar flexion torques × three knee extensor activation levels) conditions ($P < 0.05$, for each comparison).

Discussion

Dependence of plantar flexor activities on muscle synergies

The main findings of the present study were that the variability of plantar flexor activities in the synergy-relevant subspace was larger than those in task-relevant and task-irrelevant subspaces, and the variability of muscle synergy recruitments in the task-irrelevant subspace was larger than that in the task-relevant subspace. These findings suggest the dependence of plantar flexor activities on muscle synergies with holding the uncontrolled manifold principle.

A previous study reported that the variability of the EMGs of index finger muscles in the task-irrelevant subspace was larger than that in the task-relevant subspace, and insisted that this result provided the first direct evidence for the optimal feedback hypothesis at the muscle activation level (Valero-Cuevas et al. 2009). Such a larger variability of the EMGs of plantar and dorsiflexor muscles in the task-irrelevant subspace was also found in the present study, and at the same time, this variability in the task-irrelevant subspace was smaller than that in the synergy-relevant subspace (Fig. 3). Therefore, the ARVs of plantar flexor muscles depended on muscle synergies, and the large variability of the ARVs in the task-irrelevant subspace reflected the larger variability in the synergy-relevant subspace.

This study not only revealed the dependence of the ARVs of plantar flexor muscles on muscle synergies but also suggested ways in which muscle synergies are recruited. Although the variability of muscle activities in the task-irrelevant subspace was tolerated (Fig. 3), the observed drastic change in muscle activities seemingly suggested that the variability of muscle activities in the task-irrelevant subspace was controlled according to the control principle

related to knee extensor activation. This control of the variability of muscle activities was understood from the perspective of muscle synergies. The muscle synergy that had the large weightings of knee extensor muscles (e.g., *Synergy C*) contained the small weightings of plantar flexor muscles (Fig. 1). Because the recruitment of this muscle synergy increased the activities of several plantar flexor muscles at a fixed ratio, its recruitment forced changes in the recruitments of the other synergies to maintain the targeted plantar flexion torque in this study. When muscle synergy recruitments were roughly changed by a knee extension level, the variability of muscle synergy recruitments in the task-irrelevant subspace was larger than that in the task-relevant subspace at each combination of plantar flexion levels and knee extension levels (Fig. 5). This result indicated that the variability of muscle synergy recruitments was uncontrolled if it was not relevant to plantar flexion torque. In the other words, the uncontrolled manifold hypothesis was held at the muscle synergy level.

Perspective of the uncontrolled manifold principle connecting the muscle synergy level into the joint kinematics level

One of the central issues in motor control is the degrees of freedom problem (Bernstein 1967). The degrees of freedom exist at various levels, such as the joint kinematics level, the kinetics level, the muscle activation level, and the muscle synergy level. At the joint kinematics level, many previous studies reported that the joint variability irrelevant to the task goal was left according to the uncontrolled manifold principle (Diedrichsen 2007; Scholz et al. 1999, 2000). For example, at the sit-to-stand movement, the joint variance relevant to the trajectory of the center of mass of the body was smaller than the irrelevant joint variance (Scholz and Schöner 1999). To accomplish the task goal (e.g., the trajectory of the center of mass of the body) during a human voluntary movement, the central nervous system tries to correct the joint motion only if the motion error affects the task performance. According to the uncontrolled manifold

principle, the central nervous system would optimally use the feedback information that involved in the task performance, for modulating the recruitments of muscle synergies. This modulation induces successive changes at the muscle activation level (Fig. 3; Valero-Cuevas et al. 2009), the kinetics level (Scholz et al. 2002), and the joint kinematics level (Diedrichsen 2007; Scholz et al. 1999, 2000). If the uncontrolled manifold principle is fundamentally held at the muscle synergy level (Fig. 5), this principle appears at above-mentioned secondary levels.

Conclusions

The main findings of the present study were that the variability of plantar flexor activities in the synergy-relevant subspace was larger than those in task-relevant and task-irrelevant subspaces, and the variability of muscle synergy recruitments in the task-irrelevant subspace was larger than that in the task-relevant subspace. These findings suggest that plantar flexor activities depends on muscle synergies and muscle synergies are recruited according to the uncontrolled manifold principle, resulting in the uncontrolled manifold principle at the muscle activation level.

Chapter IV

Voluntary activation of triceps surae muscles depends on the presence of knee extensor activation

Introduction

Muscle force generation involves various neural pathways. For example, the maximal force generation capacity of triceps surae muscles is affected by the Ia afferent input (Ushiyama et al. 2005). At the ankle, there is reciprocal inhibition, whereby activity of dorsiflexor muscles suppresses activity of plantar flexor muscles, which act as antagonists for dorsiflexion, and vice versa (Baret et al. 2003; Nielsen et al. 1992). In multijoint lower limb movements, muscles at the knee and ankle interact with each other via transjoint neural pathways, such as facilitatory (Dyer et al. 2011; Meunier et al. 1993) and inhibitory (Meunier et al. 1994) heteronymous neural connections. The central nervous system must adequately control the neural pathways between muscles to activate each muscle.

These neural pathways, the effect of which is difficult to directly measure during voluntary motor behaviors, are involved in maximum activation of muscles. Many behavioral studies have reported that activation of muscles at a given joint was affected by the presence of muscle activities at an adjacent joint during a voluntary task (Earl et al. 2001; Fujiwara and Basmajian 1975; Gravel et al. 1987; Hodges and Richardson 1993; Yamashita 1988). For example, activity of the soleus muscle (Sol) during isometric planter flexion at 30% of the torque generated during maximal voluntary contraction (MVC) nearly doubled with simultaneous isometric knee extensor contraction (see Section I of Chapter III). Such interactions have also been reported between hip adductor and knee extensor muscles (Earl et al. 2001; Hodges and Richardson 1993; cf., Hertel et al. 2004), between hip extensor and knee extensor muscles (Fujiwara and Basmajian 1975; Yamashita 1988), and between knee flexor

and plantar flexor muscles (Gravel et al. 1987) at submaximal contraction levels. Taking into account these results, it is possible that coactivation of leg muscles is important for maximal voluntary activation. However, it has remained unclear whether and how coactivation of muscles at various leg joints can increase the maximal voluntary force generation capacity of each muscle. Recent studies (Cheung et al. 2005; Torres-Oviedo et al. 2006; Tresch et al. 1999) have quantified coactivation or interaction between muscles by computational decomposition techniques, such as non-negative matrix factorization (NMF). A combination of NMF and the interpolated twitch technique could reveal the effect of the interaction between muscles on individual muscle activation in multijoint movements that require maximal force production.

We hypothesized the increased activation of plantar flexor muscles induced by knee extensor activation would enhance plantar flexion torque. To test this hypothesis, we investigated the interactions between plantar flexor and knee extensor muscle activities and voluntary activation of triceps surae muscles during maximal voluntary isometric plantar flexion with or without knee extensor contraction using NMF and the interpolated twitch technique.

Methods

Subjects

Nine male volunteers participated in the experiment. The mean ± standard deviation age, height, and body mass of the subjects was 22.2 ± 2.8 years, 171.9 ± 5.9 cm, and 68.4 ± 9.8 kg, respectively. No subject had any significant medical history or any signs of a neurological disorder. All subjects gave their written informed consent to participate in the study after receiving a detailed explanation of the purposes, potential benefits, and risks associated with participation. The Human Research Ethics Committee at Kanagawa University approved all

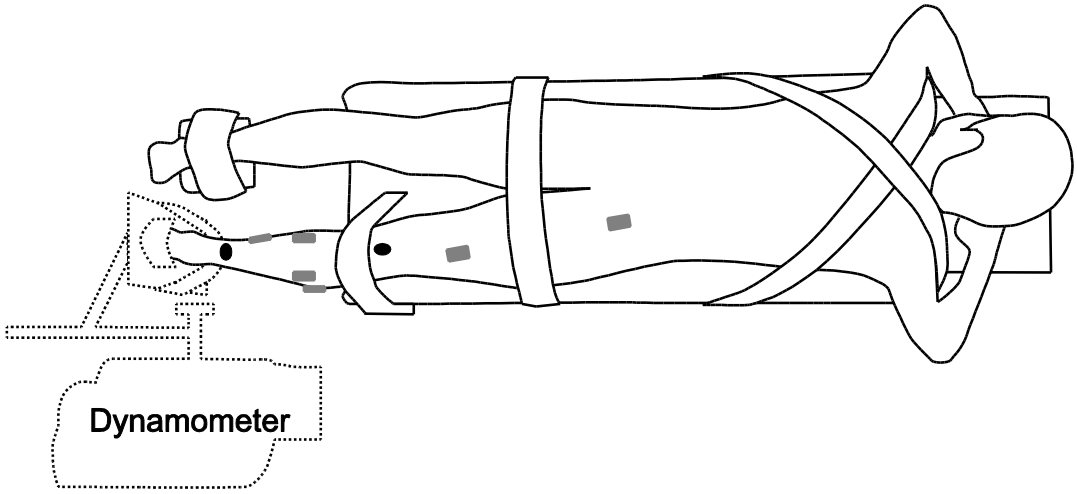

Fig. 1. Experimental setup. The dotted lines represent the dynamometer. The gray rectangles are electrodes. The black ellipses are the cathode at the popliteal fossa and the anode at the distal portion of triceps surae muscles. The electrodes on vastus lateralis and tibialis anterior muscles and the ground electrode are hidden underneath the leg.

procedures used in the study.

Experimental setup

For all trials, the subject lay prone on a flat seat with their face turned to the left, and the body was secured with straps placed around the shoulders, hips, right knee, and left ankle to minimize changes in joint angles (Fig. 1). The right knee was fully extended and was supported by pads that elevated the knee to prevent contact between the seat and the electrode placed over the vastus lateralis muscle (VL). The right ankle was positioned at 0° (neutral) and the right foot was tightly fixed to the plate of a dynamometer (Biodex System 4, Biodex Medical Systems, Shirley, NY, USA). The axis of rotation of the dynamometer was aligned with the anatomical axis of ankle dorsiflexion and plantar flexion. The torque signal was low-pass filtered at 100 Hz by a fourth-order linear phase filter (model 3611, NF, Yokohama, Japan). The ankle and knee angles were as constant as possible throughout the experiment to remove any influence of joint angle on the electromyographic (EMG) activity of plantar flexor muscles (Cresswell et al. 1995).

Surface EMG was recorded from the VL, gluteus maximus (GM), biceps femoris (BF),

tibialis anterior (TA), peroneus longus (PL), medial gastrocnemius (MG), lateral gastrocnemius (LG), and Sol muscles of the right leg using single differential electrodes (DE-2.1, Delsys, Boston, MA, USA). Prior to electrode placement, all skin sites were carefully abraded and cleaned with alcohol. Electrode placements for muscles were in accordance with the SENIAM recommendations (Freriks et al. 1999). The ground electrode was placed on the tuberositas tibiae. The EMG signals were amplified (×100) using a standard biosignal recording system (Bagnoli Desktop EMG Systems, Delsys) and band-pass filtered at 20–450 Hz before sampling. To stimulate the tibial nerve, the cathode (19 × 36 mm) was placed on the popliteal fossa and the anode (19 × 36 mm) was placed on a distal portion of triceps surae muscles, according to the settings of Behm and colleagues (1996). These stimulating Ag-AgCl electrodes (F-150S, Nihon Kohden, Tokyo, Japan) were shifted during preliminary stimulation to determine the optimal position for the greatest peak torque. The stimulation current was increased until torque in response to doublet stimulation (two 0.2-ms pulses at 100 Hz) delivered using a constant current stimulator (DS7AH, Digitimer, Letchworth, United Kingdom) leveled off. During the stimulation trials, the current was 10 mA larger than this level to stimulate the nerve at a supramaximal level. Plantar flexion torque, EMG data, and stimulation timing were sampled at 10 kHz on the hard disk of a personal computer using a 16-bit analog-to-digital converter (PowerLab 16/35, AD Instruments, Sydney, Australia).

Experimental protocol

The experimental session consisted of MVC trials followed by stimulation trials in which the subject was required to generate a maximum isometric plantar flexion torque with or without an isometric contraction of the knee extensor muscles.

Before the experiment, subjects were familiarized with the experimental procedure. At the beginning of the session, subjects performed MVC trials for hip extension, knee extension,

knee flexion, ankle eversion, ankle plantar flexion, and ankle dorsiflexion while in the above-mentioned fixed posture (Fig. 1). The level of effort was gradually increased to a maximum to avoid an EMG burst at the start of the contraction. Verbal encouragement was provided for each MVC trial. Each MVC trial lasted >3 s. Two trials were performed for each muscle group. A rest period of >1 min was provided between consecutive MVC trials. EMG was recorded during all MVC trials, but torque was measured by the dynamometer only for the plantar flexion MVC trials. The maximum torque generated during the plantar flexor MVC trials was identified (see *Data processing*).

After a rest period of >5 min, subjects performed the stimulation trials. They performed four trial sets. For each set, they were required to generate a maximum voluntary isometric plantar flexion torque with and without isometric contraction of knee extensor muscles. These two knee extensor contraction conditions were presented in a random order within each set. They were asked to press the plate of a dynamometer in the same manner for both knee extensor contraction conditions. The level of effort was gradually increased to a maximum with verbal encouragement, and when level of effort had reached maximum, the tibial nerve was stimulated by a doublet (112.2 ± 54.7 mA) for the interpolated twitch (see below), and then all muscles were relaxed. Within 5 s of relaxation (Bigland-Ritchie et al. 1983), the tibial nerve was stimulated again by a doublet for the potentiated resting twitch (see below). A >5-min rest period was given between consecutive trials. The results were withheld until completion of all trials.

Data processing

Post processing of the data was performed using in-house MATLAB algorithms (version 2014a, MathWorks, Natick, MA, USA). For the MVC trials, a 250-ms analysis window was moved through the recorded data in 0.1-ms steps. For the ankle plantar flexion MVC trials, torque was

averaged over each window. MVC torque was defined as the largest of the mean values obtained from all windows over the two trials. The MVC of MG, LG, and Sol was calculated as the maximum average rectified value (ARV) of the EMG in the window in which MVC torque occurred. This analysis depends on the widespread definition that the EMG during the MVC corresponds to the MVC torque in the same moment (Disselhorst-Klug et al. 2009). For the MVC trials for hip extension, knee extension, knee flexion, ankle eversion, and ankle dorsiflexion, a 250-ms analysis window was moved through the recorded data in 0.1-ms steps and the ARV was calculated over each 250-ms window. Because the torque was not measured during the hip extension, knee extension, knee flexion, ankle eversion, and ankle dorsiflexion MVC trials, the ARV of the GM, VL, BF, PL, and TA during MVCs were determined as the largest ARV obtained from all windows over the two MVC trials for each muscle.

For the stimulation trials, the analysis program identified the time of stimulation. The average plantar flexion torque and the ARV of the EMG for each muscle were calculated over a 250-ms window before stimulation for the interpolated twitch and expressed as a percentage of the corresponding value during MVC (%MVC). The interpolated twitch was defined as the increase in torque from the value 0.1 ms before the first doublet stimulation to the maximum within 200 ms after the first doublet stimulation. The resting twitch was defined as the increase in torque from the value 0.1 ms before the second doublet stimulation to the maximum within 200 ms after the second doublet stimulation. Voluntary activation was calculated with the following equation (McKenzie et al. 1992): voluntary activation (%) = 100 × (1 – interpolated twitch/resting twitch). To remove the influence of trial order (e.g., first or last trial) on motivation, first and last trial sets were not analyzed. Because the subjects occasionally failed to relax their muscles during stimulation for the resting twitch, a satisfactory trial set in which muscles were less active at the time of stimulation for the resting twitch was selected for the analysis from the second and third trial sets.

NMF procedure

The muscle synergy hypothesis is that each muscle belongs to one or more small modules, which are termed muscle synergies, and activation of a muscle is determined by combination of muscle synergies (Tresch et al. 1999). In the present study, coactivation effect or interaction was evaluated as a muscle synergy. The ARV of all muscles were combined into a $m \times r$ matrix (EMG_o), where m indicates the number of muscles (i.e., 8) and r indicates the number of conditions multiplied by the subject number (i.e., 18). For each subject, the NMF algorithm (Lee and Seung 2001) was applied to EMG_o (8×18 matrix). In the NMF procedure, the number of muscle synergies, s, was preset, and the adequate number was determined based on the similarity of muscle synergies (see below) after all calculations based on each number (s). Based on each preset number of synergies (s), the NMF found the properties of the synergies by populating two matrices: an $8 \times s$ matrix, which specified the relative weighting of muscles in each synergy, and an $s \times 18$ matrix, which specified the recruitment of each synergy in each condition. When these two matrices were multiplied, an 8×18 matrix (EMG_r) was produced that attempted to reconstruct EMG_o. Within this framework, the NMF performed an iterative optimization from various random initial values until it converged on two matrices that minimized the sum of the squared errors: $\sum(EMG_o - EMG_r)^2$.

The similarity of muscle synergies (Cheung et al. 2005) was calculated to determine the adequate number of synergies (the left panel of Fig. 2). First, the number of synergies were set one and two, and the NMF was performed at both preset numbers. The norm of each synergy weighting vector was normalized to one, and then scalar products between the synergy extracted by the NMF where the preset number of synergies was one (termed “one-synergy NMF” in the following text, and same terminology was applied to the other preset numbers) and the two synergies extracted by the two-synergy NMF were calculated. These two scalar products were

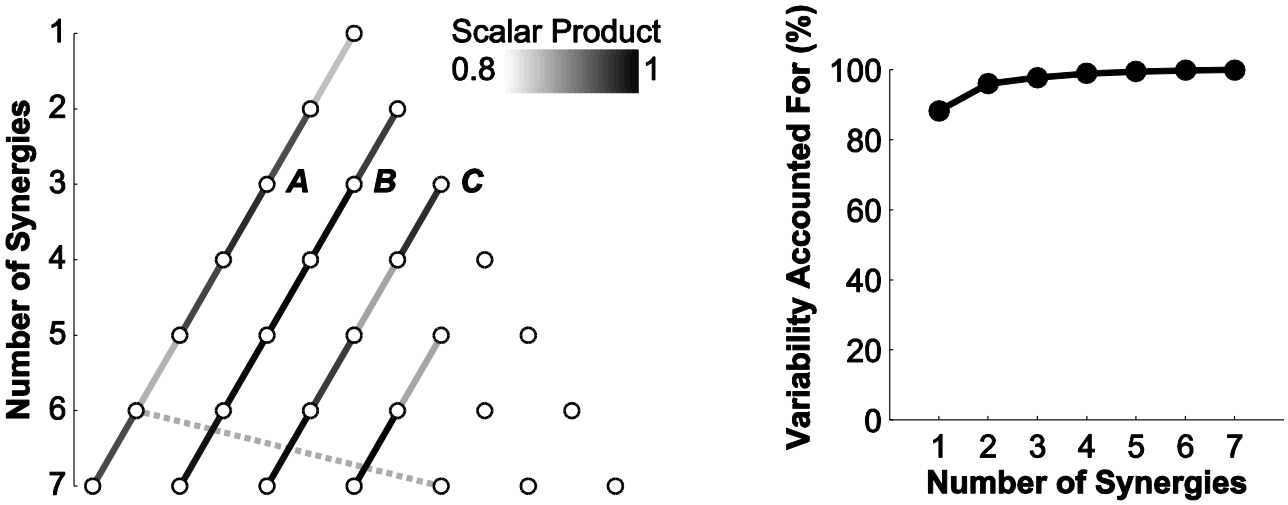

Fig. 2. Degree of data reconstruction by the non-negative matrix factorization. *Left*: Degree of similarity between muscle synergies of the contiguous non-negative matrix factorization. Open circles represent a muscle synergy extracted by the non-negative matrix factorization with each preset number of synergies. A pair of similar muscle synergies with a scalar product that exceeds 0.845 is connected by a line whose depth of color is proportional to the scalar product. The dotted line represents second similar pair. *A*, *B*, *C*: *Synergies A*, *B*, and *C* assigned in the text. *Right*: Variability accounted for based on the number of muscle synergies extracted by the non-negative matrix factorization.

averaged to define the threshold of the similarity. From one-synergy to seven-synergy NMF, the scalar product of each pair of normalized synergies between the NMFs with contiguous numbers (e.g., four-synergy and five-synergy NMFs) was calculated. If a scalar product exceeded the threshold, those synergies were "similar". When some synergies (e.g., synergies extracted by the four-synergy NMF) did not have any similar next synergies (i.e., synergies extracted by the five-synergy NMF in this example) for the first time, the adequate number of synergies was determined as the number of synergies before this moment (i.e., three in this example), because we judged that the next increment in the preset number of synergies (i.e., four-synergy NMF in this example) was too much to extract a new synergy that had a persistent similarity (see Results). Additionally, to provide an indication of the adequacy of the number of synergies, the variability accounted for (Torres-Oviedo et al. 2006) was calculated as the ratio of the sum of the squared EMG_r to the sum of the squared EMG_o; variability accounted for (%) = $100 \times (\sum EMG_r^2 / \sum EMG_o^2)$.

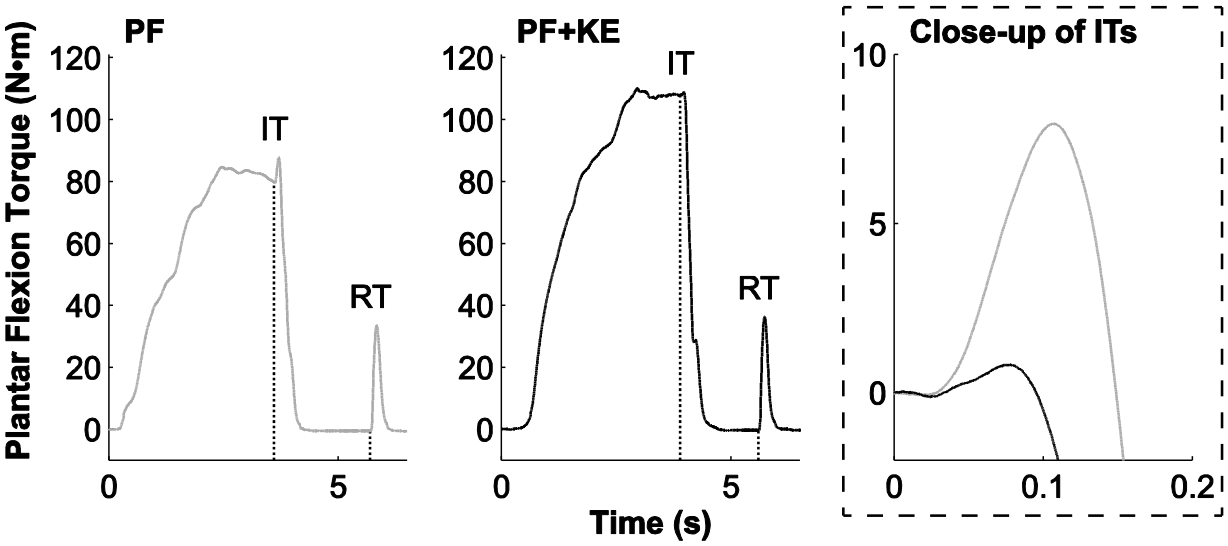

Fig. 3. Example plantar flexion torque during stimulation trials. *Left*: Torque during plantar flexion (PF; gray line). *Middle*: Torque during plantar flexion with knee extension (PF+KE; black line). *Right*: Interpolated twitch extracted from both conditions on an expanded scale. The dotted lines represent the timing of electrical stimulation for the interpolated twitch (IT) and the resting twitch (RT). In the right panel, the vertical axis is the plantar flexion torque relative to the value 0.1 ms before the first electrical stimulation, and the horizontal axis is the time relative to the first electrical stimulation.

Statistics

The plantar flexion torque and all the ARVs (expressed as %MVC) before stimulation for the interpolated twitch, the voluntary activation, and the recruitment of each muscle synergy were compared between knee extensor contraction conditions (with or without knee extensor contraction) using a paired *t*-test. With R software (version 3.1.1, R Core Team 2014), a paired *t*-test was performed, and the effect size (Cohen's *d*) and 95% confidence interval (95% CI [Lower limit, Upper limit]) were calculated. The level of significance for all comparisons was set at $P < 0.05$.

Results

A typical example of the plantar flexion torque during a stimulation trial is shown in the left and middle panels of Figure 3, and the interpolated twitches in both knee extension conditions are shown on an expanded scale in the right panel of Figure 3. Consistent with this typical example, the plantar flexion torque was significantly increased with knee extensor contraction

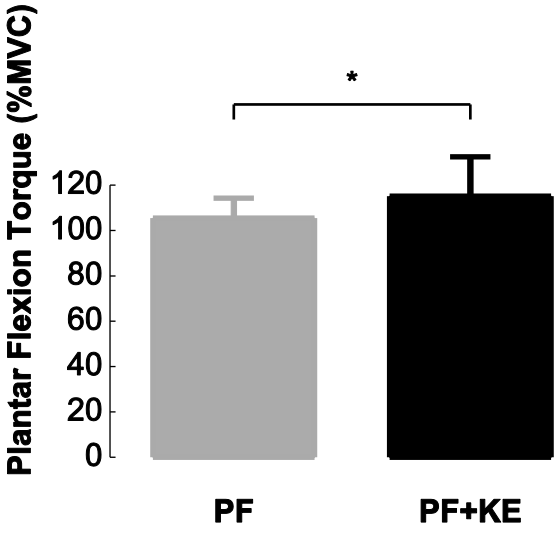

Fig. 4. Exerted plantar flexion torque during the stimulation trials. The data and error bars indicate the mean and standard deviation, respectively. %MVC: plantar flexion torque is expressed as a percentage of the corresponding value during maximal voluntary contraction; PF: plantar flexion; PF+KE: plantar flexion with knee extension. A significant difference is indicated: * $P < 0.05$.

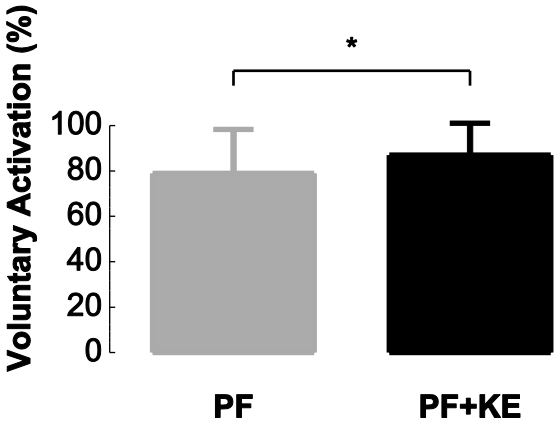

Fig. 5. Voluntary activation of plantar flexor muscles during the stimulation trials. The data and error bars indicate the mean and standard deviation, respectively. Voluntary activation was calculated using the following equation: voluntary activation (%) = 100 × (1 – interpolated twitch/resting twitch). PF: plantar flexion; PF+KE: plantar flexion with knee extension. A significant difference is indicated: * $P < 0.05$.

Table 1. Average rectified values (ARV) of electromyographic activity of muscles in stimulation trials

	ARV (%MVC)		t_8	P	d	95% CI
	PF	PF+KE				
VL	10.8 (16.0)	38.2 (17.1)	4.02	**0.0039**	1.65	[11.68, 43.14]
GM	13.1 (15.7)	23.5 (20.0)	2.88	**0.0204**	0.58	[2.08, 18.68]
BF	24.8 (19.0)	14.8 (10.5)	-2.56	**0.0335**	0.66	[-19.09, -1.01]
TA	7.9 (3.1)	8.8 (2.9)	1.44	0.1867	0.31	[-0.56, 2.43]
PL	93.2 (46.3)	104.1 (52.8)	2.24	0.0557	0.22	[-0.34, 22.33]
MG	95.9 (16.5)	114.2 (21.0)	3.04	**0.0162**	0.97	[4.39, 32.13]
LG	101.7 (33.1)	135.5 (88.9)	1.42	0.1927	0.50	[-20.97, 88.51]
Sol	103.8 (41.7)	131.2 (40.7)	2.42	**0.0421**	0.67	[1.25, 53.68]

The ARV data are mean (standard deviation). P values that are < 0.05 appear in bold. VL: vastus lateralis; GM: gluteus maximus; BF: biceps femoris; TA: tibialis anterior; PL: peroneus longus; MG: medial gastrocnemius; LG: lateral gastrocnemius; Sol: soleus; %MVC: a percentage of the corresponding value during maximal voluntary contraction; PF: plantar flexion; PF+KE: plantar flexion with knee extension; t_8: t value (eight degrees of freedom); d: Cohen's d; 95% CI [Lower limit, Upper limit]: 95% confidence interval.

(t_8 = 2.32, P = 0.0492, d = 0.71, 95% CI [0.04, 19.38]; Fig. 4). Compared to plantar flexion alone, the interpolated twitch amplitude appeared lower with simultaneous plantar flexion and knee extension (Fig. 3), indicating that voluntary activation of triceps surae muscles was increased. Indeed, across the group as a whole, voluntary activation was significantly increased with knee extensor contraction (t_8 = 2.90, P = 0.0201, d = 0.48, 95% CI [1.65, 14.48]; Fig. 5). With knee extensor contraction, the ARVs of the VL, GM, MG and Sol were significantly increased whereas the BF ARV was significantly decreased (Table 1).

The relation between the number of muscle synergies and the similarity of synergies is shown in the left of Figure 2. Scalar products between the normalized synergy weighting vector of the one-synergy NMF and the two normalized synergy weighting vectors of the two-synergy NMF were 0.85 and 0.84. Therefore, the averaged value was 0.845, and a pair of similar muscle synergies with a scalar product that exceeds 0.845 is connected by a line whose depth of color is proportional to the scalar product. Comparing the results of the four-synergy NMF with that of the five-synergy NMF, one synergy of the four-synergy NMF did not have any similar synergies to the five-synergy NMF. Additionally, the increase in the variability accounted for seemed to plateau at the three-synergy NMF (Fig. 2, right panel). Therefore, the adequate number of synergies was determined as three, and the three extracted synergies were labeled *Synergy A*, *B*, and *C*.

The recruitment of *Synergy A*, which mainly had high weightings for monoarticular plantar flexor muscles such as the PL and Sol (Fig. 6), and that of *Synergy B*, which had large weightings for biarticular plantar flexor muscles such as the MG and LG, did not significantly change with knee extensor contraction (t_8 = -1.69, P = 0.1304, d = 0.14, 95% CI [-56.72, 8.82]; t_8 = 0.40, P = 0.6989, d = 0.14, 95% CI [-96.97, 137.78], respectively). On the other hand, the recruitment of *Synergy C*, which had weightings for both knee extensor and plantar flexor muscles, significantly increased with knee extensor contraction (t_8 = 4.11, P = 0.0034, d = 1.02,

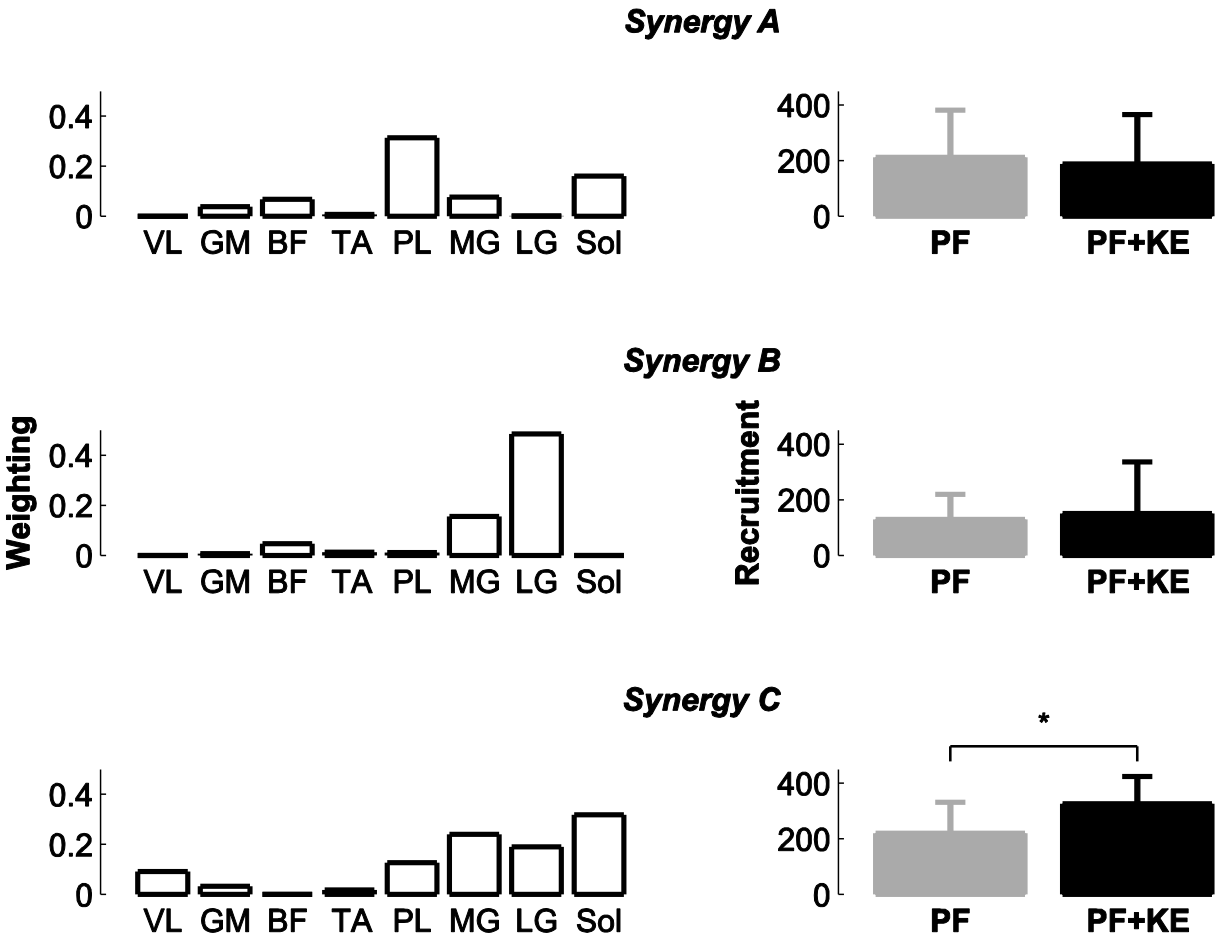

Fig. 6. Weightings and recruitments of muscles synergies extracted by the non-negative matrix factorization. *Left*: Weightings of muscle synergies. *Right*: Average recruitment of muscle synergies. The error bars indicate the standard deviation. VL: vastus lateralis; GM: gluteus maximus; BF: biceps femoris; TA: tibialis anterior; PL: peroneus longus; MG: medial gastrocnemius; LG: lateral gastrocnemius; Sol: soleus; PF: plantar flexion; PF+KE: plantar flexion with knee extension. The weighting and recruitment are expressed in arbitrary units. A significant difference is indicated: * $P < 0.05$.

95% CI [47.03, 166.95]; Fig. 6).

Discussion

Voluntary activation of triceps surae muscles

The main finding of the present study was that coactivation of plantar flexor and knee extensor muscles and voluntary activation of triceps surae muscles were increased with knee extensor contraction, resulting in an increase in the voluntary plantar flexion torque. On average, the 8.1 percentage point increase in voluntary activation almost corresponded to the 9.7% MVC

increase in plantar flexion torque. These findings suggest that simultaneous knee extensor activation was important for maximum force generation of triceps surae muscles.

It has previously been observed that single-joint knee extension accompanied unconscious activation not of plantar flexor muscles, such as the MG and Sol, but of dorsiflexor muscles, such as the TA (Aruin 2001). Because of the antagonistic function of the TA for plantar flexion, unconscious activation of the TA reduced the efficiency of multijoint contraction of plantar flexor muscles and knee extensor muscles. Actually, in the present study, knee extensor contraction did not induce a change in TA activity, but increased MG and Sol activities (Table 1). Coactivation of plantar flexor muscles and knee extensor muscles was selected for a given multijoint task, and the recruitment of this coupling led to higher voluntary activation of triceps surae muscles (Fig. 5).

Some previous studies have reported that it is difficult to activate triceps surae muscles to the maximum by volition (Belanger and McComas 1981; Bigland-Ritchie et al. 1986). For example, voluntary activation of triceps surae muscles was 70–100% during voluntary isometric plantar flexion even at 100% of the MVC torque, whereas dorsiflexor muscles were almost fully activated during isometric dorsiflexion at more than 80% of the MVC torque (Belanger and McComas 1981). In the present study, average voluntary activation of triceps surae muscles was low during maximal plantar flexion alone (78.9%) and increased to 87.0% with simultaneous knee extension contraction (Fig. 5). However, the recruitment of *Synergy A* and *B* did not significantly change (Fig. 6), indicating that the voluntary effort that was not related to the VL achieved the maximum level during plantar flexion alone. Because it was only the recruitment of *Synergy C*, which included plantar flexor and knee extensor muscles, that increased with knee extensor contraction (Fig. 6), the increase in plantar flexor activation could be explained by coactivation or the interaction between these muscles that occurs during multijoint tasks. From the perspective of muscle synergies (Tresch et al. 1999), it is possible

that plantar flexor muscles belong to synergies specialized for plantar flexor muscles and are also grouped with knee extensor muscles in another synergy. If synergies make it difficult to specifically activate each muscle to the maximum (Aruin 2001; Hwang and Abraham 2001), plantar flexion alone could not recruit all muscle synergies required for maximal activation of plantar flexor muscles. On the other hand, simultaneous plantar flexion and knee extension could recruit one more muscle synergy, and then plantar flexor muscles are more activated. Consequently, simultaneous knee extensor activation was important for the highest voluntary activation of triceps surae muscles and the maximum resultant plantar flexion torque (Fig. 4).

Practical significance

Simultaneous motion of plantar flexion and knee extension is required for various sporting activities, such as jumping (Iida et al. 2012) and sprinting (Ball and Scurr 2010), and large muscle activation has been reported in these activities. For example, MG and Sol activities during squat jumping or sprinting were larger than those during fast isolated isokinetic plantar flexion at maximum effort (Ball and Scurr 2010). Coactivation of plantar flexor muscles and knee extensor muscles would contribute to such an increase in MG and Sol activities during a multijoint movement compared to a single-joint movement. The observed coactivation system is available for multijoint movements beyond the static situation in this study.

Simultaneous knee extensor contraction induced an increase in activation of not only the Sol but also the MG, which also anatomically functions as an antagonist for knee extension (Table 1). This somewhat contradictory activation of the MG would efficiently enhance a plantar flexion torque in practical situations. Knee extensor muscles have larger volumes than plantar flexor muscles (Friederich and Brand 1990), and pull on the calcaneus secondary to the action of biarticular plantar flexors. In this way, they accelerate the ankle to plantar flexion (Prilutsky and Zatsiorsky 1994). Such a mechanical property for straightening of a leg favors

coactivation of knee extensor muscles and the MG.

A recent study reported inconsistent results when comparing the maximal plantar flexion torque between isolated plantar flexion and seated leg press where knee extensor muscles were coactivated (Hahn et al. 2011). Similar to the results of the present study (Fig. 4), the plantar flexion torque in the latter task was larger than that in the former task in a lengthened leg posture, but in a shortened leg posture, it was the other way around. Previous studies have revealed that control of heteronymous neural pathways from the quadriceps to ankle muscles depends on a posture (Barbeau et al. 2000). Even in isolated plantar flexion, the activation strategy of triceps surae muscles changes with the angle of the knee and ankle joints (Cresswell et al. 1995; Sale et al. 1982). For example, the maximum activities of the MG and LG at a knee angle of 60 degrees were less than 40% of those at a knee angle of 180 degrees (Cresswell et al. 1995). Voluntary activation of triceps surae muscles decreased with a greater plantar flexion angle (Sale et al. 1982). Although the present study revealed that simultaneous contraction of knee extensor muscles leads to higher force generation by the MG and Sol when the knee is fully extended and the ankle neutral, future studies on the effect of knee extensor activation in various postures are necessary to confirm the practical significance of this phenomenon.

Limitations

Although the increase in voluntary activation of plantar flexor muscles almost corresponded to the increase in torque with simultaneous knee extensor contraction, the increase in MG and Sol activities (18.3% and 27.4% MVC, respectively; Table 1) were somewhat higher than the 8.1 percentage point increase in voluntary activation (Fig. 5). However, plantar flexor muscles other than triceps surae muscles contribute at least 20% of the plantar flexion torque (Murray et al. 1976). Among these other muscles (e.g., plantaris, peroneus brevis), only PL activity was recorded in the present study and this was not significantly changed with simultaneous knee

extensor contraction. It is possible that the unrecorded activities of other plantar flexor muscles also did not increase, similar to PL activity. In addition, muscle activities at a high intensity generate a less torque than that expected because the EMG-torque relation is non-linear (Cresswell et al. 1995; Disselhorst-Klug et al. 2009). Consequently, an increase in MG and Sol activity is consistent with an increase in voluntary activation.

Dissimilar to MG activity, LG activity did not significantly change with knee extensor activation. In this study, the standard deviation of LG activity during plantar flexion with knee extensor activation was large (Table 1). A previous study also reported that the average LG activity during single-leg plantar flexion during standing, where knee extensor muscles would be coactivated, was about 100% MVC and the standard deviation across subjects was about 80% MVC (Wolf et al. 1993). These results indicate that the effect of knee extensor activation on LG activity differed substantially between individuals.

An increase both in Sol and MG activities at maximal plantar flexion in this study somewhat contradicts the results of our previous study at submaximal contraction levels. During plantar flexion at a preset constant torque level ranging from 10 to 30% MVC, knee extensor activation induced an increase in Sol activity and a decrease in MG activity (see Section I of Chapter III). In this task, an increase in Sol activity requires a decrease in the activity of other plantar flexor muscles to maintain a constant plantar flexion torque. The facilitatory heteronymous connection from the quadriceps muscles to the Sol is so primitive that it exists not only in humans, who have several transjoint neural pathways (Meunier et al. 1993), but also in animals, such as the cat and baboon, which have few transjoint neural pathways between the knee and ankle (Eccles et al. 1957; Hongo et al. 1984). Although a facilitatory connection from the quadriceps muscles to the MG also exists (Meunier et al. 1993), the relation of the quadriceps muscles to the Sol might be stronger than that to the MG and, if so, the submaximal task would have obscured the influence of knee extensor activation on MG activity.

Conclusions

The present study revealed that voluntary activation of triceps surae muscles, especially the MG and Sol, was increased with coactivation of knee extensor muscles, resulting in an increase in the voluntary plantar flexion torque. These results suggest that simultaneous knee extensor activation is important for the highest voluntary activation of triceps surae muscles and the maximum resultant torque.

Chapter V

General Discussion

Dependence of human motor control on muscle synergies

The main purpose of the thesis is to confirm the dependence of human motor control on muscle synergies. For this purpose, various patterns of plantar flexor activities at the mechanically same condition were quantified.

In the behavioral approach based on computational decomposition techniques, such as the non-negative matrix factorization (Lee and Seung 1999), previous studies evaluated muscle activities during various movements (Cappellini et al. 2006; d'Avella et al. 2003; Roh et al. 2011; Tresch et al. 1999) or a dynamic movement which included tonic and silent periods of individual muscle activities, such as walking (Clark et al. 2010; Dominici et al. 2011). These studies extracted muscle synergies from resultant muscle activities, based on the premise that various muscle activation patterns were feasible for these movements. However, a given movement largely reduces feasible muscle activation patterns (Kutch and Valero-Cuevas 2012; Tresch and Jarc 2009). Partly because of reduction in feasible patterns at a given movement, computer simulation studies based on minimizing an objective function, such as the metabolic energy (Anderson and Pandy 2001) or the weighted squared sum of muscle forces (Xiao and Higginson 2008), predicted synergy-like grouped muscle activities regardless of no assumption to muscle synergies. In another aspect, the electromyographic analysis is difficult to evaluate the dynamic movements, which many synergy studies have investigated, because of the signal nonstationarity, the shift of the electrodes relative to muscle fibers, and the changes in the conductivitiy properties of the tissues separating electrodes and muscle fibers (Farina 2006). Even though previous studies aimed to extract a relatively small number of grouped muscle

activities from various patterns, feasible muscle activation patterns that the mechanical constraints reduced might be misinterpreted as muscle synergies because the actual number of feasible activation patterns was unknown at a given movement. This lack of information prevented previous studies in the behavioral approach from strictly examining the dependence of human motor control on muscle synergies.

In contrast to previous studies, isometric plantar flexion with or without isometric knee extension in this research clearly required only one mechanical constraint. Because the mechanical constraint of this research was plantar flexion torque only and was not affected by knee extension at fully extended knee position, the mechanical constraint was same under a given plantar flexion torque regardless of knee extensor activation. When the slope of regression line, which suggested a muscle synergy (Lee 1984), between plantar flexor activities was drastically changed with knee extensor activation (Chapter II, and Section II of Chapter III), the number of constrained muscle activation patterns exceeded that of mechanical constraints. Therefore, this result suggests that plantar flexor activation is non-mechanically constrained.

Non-mechanical constraints correspond to not only muscle synergies but also the peripheral neural pathways between knee extensor and plantar flexor muscles (Meunier et al. 1993, 1994). For example, the heteronymous connection from the quadriceps muscles to the soleus muscle (Meunier et al. 1993) would increase the soleus activity with adding knee extensor activation to plantar flexion, and then, the activation ratio between the soleus muscle and other plantar flexor muscles, such as medial and lateral gastrocnemius, and peroneus longus and brevis muscles, must change to maintain the targeted torque. Certainly, knee extensor activation at low-intensity plantar flexion induced an increase in the soleus activity and a decrease in the medial gastrocnemius activity (Section I of Chapter III). However, increasing knee extensor activation from 50% to 100% of the maximum still induced an increase in the soleus activity but did not decrease the gastrocnemius activity (Chapter II and Section I of

Chapter III) and rather increased the medial gastrocnemius activity during plantar flexion at the level of 20% of the maximum torque (Chapter II). At high-intensity plantar flexion, knee extensor activation at any levels had a facilitatory effect on the medial gastrocnemius activity (Chapter II). To explain these phenomena through the peripheral neural pathways from the quadriceps muscles, various situation-dependent effects of these pathways are necessary. Alternatively, the muscle synergy hypothesis allows a better view that planar flexor activities are changed by recruited plantar flexor synergies depending on the presence of knee extensor activation. By the non-negative matrix factorization (i.e., Chapter II to IV except for Section I of Chapter III), an interaction between knee extensor and plantar flexor muscles was extracted as the simultaneous weightings of these muscles in one muscle synergy vector. At the same time, Chapter II revealed that this interaction was not enough to explain a drastic change in the activation ratio between plantar flexor muscles. As demonstrated in Chapter II, if only one muscle synergy that had large weightings of knee extensor muscles and smaller weightings of plantar flexor muscles was additively recruited, the regression line that represented the activation ratio between plantar flexor muscles would be parallel-shifted. Therefore, one knee extensor synergy and two muscle synergies that had large weightings of plantar flexor muscles were necessary to explain a drastic change in plantar flexor activities induced by knee extensor activation. Then, more than one muscle synergy to which plantar flexor muscles mainly belong exceeded that of the mechanical constraint (i.e., the plantar flexion torque). This analysis provided one of the direct evidence of the dependence of lower limb control on muscle synergies.

Uncontrolled manifold hypothesis at the muscle synergy level

A recent study had applied the uncontrolled manifold approach to the muscle activation level and reported that the variability of index finger muscle activities that affected the fingertip force was smaller than their task-irrelevant variability (Valero-Cuevas et al. 2009). One interpretation

(Tresch and Jarc 2009) is that this small variability suggests that each muscle was independently controlled and its activity that did not affect the task (i.e., fingertip force) was uncontrolled. This interpretation emphasizes the independent control of muscle activities and seemingly contradicts the muscle synergy hypothesis (Tresch et al. 1999). However, Section II of Chapter III revealed that the uncontrolled manifold hypothesis does not contradict the muscle synergy hypothesis. A larger variability of plantar and dorsiflexor activities in the task-irrelevant subspace was also found, and at the same time, this variability in the task-irrelevant subspace was smaller than that in the synergy-relevant subspace (Fig. 2 in Section II of Chapter III). Because the large variability of their activities in the task-irrelevant subspace reflected their larger variability in the synergy-relevant subspace, plantar flexor activities still depended on muscle synergies with holding the uncontrolled manifold principle at the muscle activation level.

The uncontrolled manifold principle does not contradict but would rather correspond to the muscle synergy recruitment strategy itself. At each condition in Section II of Chapter III, the variability of muscle synergy recruitments in the task-irrelevant subspace was larger than that in the task-relevant subspace (Fig. 4 in Section II of Chapter III). This result indicated that the variability of muscle synergy recruitments was controlled only if it was relevant to the plantar flexion torque. In the other words, the uncontrolled manifold principle was held at the muscle synergy level. The present research not only revealed the dependence of lower limb control on muscle synergies but also suggested the recruitment strategy of muscle synergies.

Previous studies have revealed the physiological entity for linear muscle activation and linear combination of activation, which were premised by the muscle synergy hypothesis. The orderly recruitment of motoneurons depending on the size principle (Henneman et al. 1965) would result in linear muscle activation. Motoneurons innervating a given muscle would be divided into termed task groups (Loeb 1985), and the size principle is held within each task group (Riek and Bawa 1992). A task group would be formed across different muscles (Sokoloff

et al. 1999; Wyman et al. 1974), through a spinal interneuron (Bizzi et al. 1991; Takei and Seki 2010) or a cortical interneuron with corticomotoneuronal cells (Huntley and Jones 1991). A muscle synergy could be expressed as such a task group. Summation of recruitments of muscle synergies enables linear combination of muscle activation. Although muscle synergies could correspond to the above-mentioned physiological systems, the recruitment strategy of muscle synergies remained unclear (Sokoloff et al. 1999). The uncontrolled manifold analysis for the muscle synergy recruitment provided a new insight into this physiologically unsolved problem for the muscle synergy hypothesis.

Determination of the recruitment ratio among muscle synergies when changing a task

Chapter II reported the different effect of knee extensor activation on plantar flexor activities between low and high intensities. At low-intensity plantar flexion, the slope of regression line between plantar flexor activities was drastically changed with knee extensor activation (Chapter II, and Section II of Chapter III). On the other hand, the slope of regression line did not show a marked change with knee extensor activation during high-intensity plantar flexion (Chapter II). This discrepancy would come in the relative impact of the recruitment of a muscle synergy that had the large weightings of knee extensor muscles and the small weightings of plantar flexor muscles.

With knee extensor activation, an increase in the soleus activity was about 30% of the maximum (Chapter II and Section I of Chapter III). During low-intensity plantar flexion, the activity of other plantar flexor muscles, such as the medial gastrocnemius muscle, should decrease to maintain the constant low-level plantar flexion torque. From the perspective of muscle synergies for this phenomenon, when adding knee extensor activation to plantar flexion, knee extensor muscles and some plantar flexor muscles are coactivated by a muscle synergy that has both weightings. This coactivation forces a drastic change in the recruitment ratio

among muscle synergies, compared to plantar flexion alone. On the other hand, the impact of the soleus activity increased by knee extensor activation is relatively small during high-intensity plantar flexion because the soleus activity has already been high before adding knee extensor activation (Chapter II). A subtle change in the recruitment ratio among related muscle synergies is enough to combine the interaction effect from knee extensor activation, which is represented as a muscle synergy, into generation of the targeted torque at high-intensity plantar flexion, and then, the slope of regression line between plantar flexor activities does not drastically change.

Adding knee extensor activation to high-intensity plantar flexion did not induce a clear change in the recruitment of muscle synergies to which plantar flexor muscles mainly belong, but still, plantar flexor activities were affected by knee extensor activation. In Chapter IV, plantar flexion alone seemed to fully recruit the muscle synergies that had large weightings of plantar flexor muscles. When adding knee extensor activation to plantar flexion, voluntary activation of triceps surae muscles evaluated by their electromyographic activities and the interpolated twitch technique was increased, resulting in a higher plantar flexion torque. This phenomenon was simply explained by the recruitment of the muscle synergy that had weightings of knee extensor muscles and plantar flexor muscles.

Perspective for human movements

Muscle synergies could reduce the degrees of freedom of lower limb muscles or motor units. Especially, the central pattern generator could generate locomotion (Grillner and Zangger 1975) by using such simplified modules (Taga et al. 1991). If the number of plantar flexor synergies is one as in the case of previous muscle synergy studies that set the arbitrary criterion for determining the number of muscle synergies (Cappellini et al. 2006; Clark et al. 2010; Dominici et al. 2011), the lower limb control is simplest. However, the present research suggested that more than one plantar flexor synergy left the degrees of freedom and the recruitment strategy

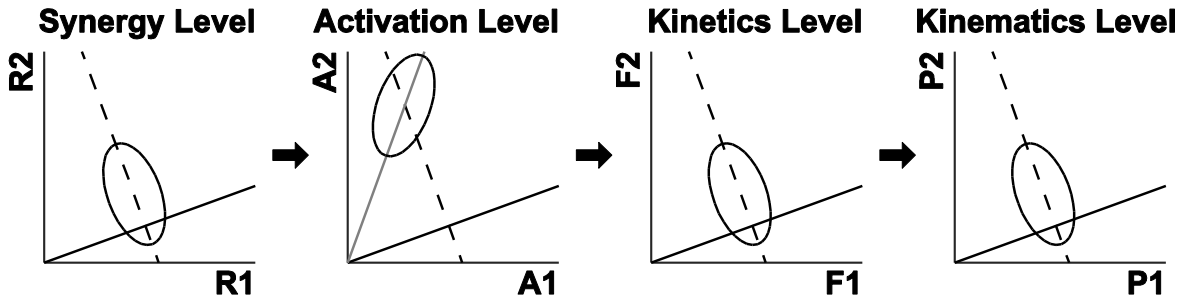

Fig. 1. Schematic illustration of the uncontrolled manifold at all levels. The black solid line, the dashed line, and the grey solid line represent the task-relevant, task-irrelevant, and synergy-relevant subspace, respectively. R: recruitment; A: activation; F: force; P: position.

of muscle synergies was somewhat non-deterministic according to the uncontrolled manifold principle.

The uncontrolled manifold hypothesis has proposed that the variability that influences the task performance is corrected but the other variability is left (Schöner 1995). This hypothesis has been confirmed at the joint kinematics level (Scholz and Schöner 1999), the kinetics level (Scholz et al. 2002), and the muscle activation level (Valero-Cuevas et al. 2009). As above mentioned, the present research updated the uncontrolled manifold hypothesis at the muscle activation level (the second panel from the left of Fig. 1 of this Chapter) and first suggested the uncontrolled manifold principle at the muscle synergy level (the leftmost panel of Fig. 1 of this Chapter).

To accomplish the task goal during a human voluntary movement, the central nervous system tries to correct the joint motion only if the motion error affects the task performance, and if not, the error from the desired trajectory is neglected. According to the uncontrolled manifold principle, the central nervous system optimally uses the feedback information that involved in the task performance, for modulating the recruitments of muscle synergies. This modulation induces successive changes at the muscle activation level (Fig. 3; Valero-Cuevas et al. 2009), the kinetics level (Scholz et al. 2002), and the joint kinematics level (Diedrichsen 2007; Scholz et al. 1999, 2000). Because the uncontrolled manifold principle is fundamentally held at the muscle synergy level (Fig. 5 in Section II of Chapter III), this principle would appear

at these secondary levels.

Conclusions

The present research confirmed the dependence of human motor control of plantar flexor activities on muscle synergies, with clarifying the mechanical constraint and suggested that the muscle synergy recruitment strategy within a task corresponds to the uncontrolled manifold principle, leading to the uncontrolled manifold principle at the muscle activation level and other secondary levels.

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