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Analysis of increasing and decreasing isometric finger force generation and the possible role of the corticospinal system in this process

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Abstract

This study investigated the possible role of the corticospinal system during force generation and force relaxation. Nine young and healthy subjects were instructed to produce a total force with four fingers within a hand following a preset force generation and relaxation ramp template closely. Excitability of corticospinal (CS) projections was assessed by single- and paired-pulse TMS. Errors introduced by a finger force were partially compensated by other finger forces during force generation, but were amplified during force relaxation. The CS excitability was greater during force generation than maintenance or relaxation. No difference in intracortical inhibition or facilitation was found. Non-normalized finger extensor EMG responses remained unchanged. The findings suggest that force relaxation is not just a withdrawal from activation, and multi-finger interactions are likely controlled beyond the primary motor cortex.

Keywords

synergy; finger; force; force relaxation; TMS

Introduction

When subjects generate a precisely controlled force following a preset ramp template with multiple fingers within a hand, finger forces are usually organized in such a way that they compensate for each other's errors to match the preset ramp precisely. In other words, increase in finger force by one finger is compensated by decreased forces of another finger(s). Therefore, each finger preserves a certain degree of freedom in force production (i.e., physiological independence during multi-finger force production (Danion et al. 2003)), while the error of total force during ramp matching is minimized, i.e., the sum of variances of each finger force (Sum_Var) is greater than the variance of total force (Var_Tot). This phenomenon of multi-finger interactions is called a multi-finger synergy (Latash 2010; Latash et al. 1998, 2002, 2008). The multi-finger synergy is organized centrally (Latash et al. 2005) with hierarchies (Latash 2010), and is able to adjust in response to practice (Latash et al. 2003; Latash et al. 2003), fatigue (Kruger et al. 2007; Singh et al. 2010) and aging (Olafsdottir et al. 2008; Park et al. 2011). A previous study reported the ability of error compensation among digits was better during multi-digit force generation than force

voluntary relaxation (Shim et al. 2005). No difference in performance during pinch force generation and relaxation (decrease) was reported in another study (Spraker et al. 2009).

Voluntary relaxation is as important as voluntary force generation during voluntary movement, for example, handling of fragile objects or releasing from a firm grip. When instructed to following a preset visual target, subjects usually have larger performance variability in the force relaxation phase than in the force generation phase. The observation has been reported in young, elderly and stroke subjects (Naik et al. 2011; Orizio et al. 2010; Voelcker-Rehage & Alberts 2005). In a recent functional MRI (fMRI) study (Spraker et al. 2009) that compared precisely-controlled force generation and relaxation during pinching by right thumb and middle finger, Spraker et al. reported that errors of matching the ramps were similar during discrete force generation and relaxation. Although activated neural substrates (cortical and subcortical) were the same during force generation and relaxation, the authors found decreased activities in the contralateral primary motor cortex (M1), increased activation in dorsolateral prefrontal cortex (DLPFC), decreased activity in bilateral anterior cingulate cortex (ACC), and similar activities in premotor, supplement motor area (SMA) and basal ganglia during force relaxation, as compared to force generation. The pattern of difference was the same across different force magnitudes, rate of force development and relaxation. The authors inferred that force generation and relaxation may involve different mechanisms, possibly increased intracortical inhibition during force relaxation. However, Kimura et al. (Kimura et al. 2003) reported greater motor evoke potentials (MEP) during the force generation phase than the force relaxation phase during sinusoidal elbow flexion tasks. The authors ascribed the difference to hysteresis of corticospinal excitability.

This study aimed to investigate multi-finger interactions during force generation and relaxation using single- and paired-pulse TMS. The present study first compared multi-finger interactions and error compensation between force generation and relaxation by utilizing an established multi-finger ramp force production paradigm. It was hypothesized that the ability to compensate each other's errors was less during force relaxation than force generation, (cf (Naik et al. 2011; Orizio et al. 2010; Shim et al. 2005; Voelcker-Rehage et al. 2005)). The present study then compared corticospinal (CS) excitability using single-pulse TMS and intracortical activities using paired-pulse TMS between force relaxation and force generation. It was hypothesized that there was less CS excitability, greater intracortical inhibition during force relaxation than force generation (cf. (Spraker et al. 2009)).

Methods

Subjects

Nine young, healthy subjects participated in this study (5 male and 4 female; average: 32.4 years of age, ranging from 28 to 42 years old). Subjects were screened for any significant orthopedic or neurologic injury to the upper extremity impeding their ability to complete finger force production tasks. Eight subjects were right-handed and one was left-handed when observed during the signing of consent forms and by subjective reports. All subjects gave informed consent according to the procedures approved by The Institutional Review Board of the University of Texas Health Science Center at Houston and all procedures were consistent with The Declaration of Helsinki.

4.2 Experimental settings and recordings

During the experiments, the subject sat in a height-adjustable chair, with the upper arm (test side) at approximately 45° of abduction in the frontal plane and 45° of flexion in the sagittal plane, and the elbow at approximately 135° of flexion. The test forearm resting on the wooden board was stabilized using two Valcro straps at the proximal and distal forearm. The

proximal and distal interphalangeal joints were positioned into slight flexion to the degree of subject comfort and optimal force production. The wrist was maintained in slight extension (about 20°) due to the height of the force sensors position on top of the wooden board. Both the wrist and the forearm maintained contact with the wooden board during the experiment. The non-test upper extremity was placed on top of the table comfortably in a relatively symmetrical configuration.

Four unidirectional piezoelectric force sensors (model 208CO2; Piezotronic Inc.) were used to measure individual finger forces. The sensors were mounted on aluminum posts, covered with cotton pads and placed within a 90mm×140mm aluminum frame. The frame was placed into a groove in a wooden board. The frame was adjustable horizontally within the groove. The sensors were adjustable vertically within the frame to accommodate individual hand anatomy. Analog output signals from the sensors were connected to separate signal conditioners (model 484B11, PCB Piezotronics Inc., USA). Differential surface EMG electrodes (DelSys Inc., Boston, MA) were placed over the muscle bellies of the finger flexors (FDS) and finger extensors (EDC) of the right arm to obtain EMG signals. The EMG signals were amplified, digitized and high-pass filtered at 10 Hz and low pass filtered at 500 Hz. The digitized FDS and EDC EMG signals were set at a high gain (25 μ V per division) for on-line monitoring. The force and EMG signals were sampled at 1,000 Hz using a 16-bit analog-to-digital converter (PCI-6229, National Instruments, Austin, TX, USA) using customized LabView software (National Instrument, Austin, TX).

The present study consisted of two experimental sessions. The first experiment was ramp force generation and relaxation without TMS. The second experiment was with single- or paired-pulse TMS during ramp force generation, constant force maintenance and relaxation.

Exp 1. Ramp force generation and relaxation—The procedure for ramp force trials was adopted from previous studies (Kruger et al. 2007;Shinohara et al. 2003). Subjects first performed MVC tasks with all four fingers in the above-described configuration for three trials. The trial with the largest force was recorded. Trials were interspersed with 20-s rest periods to avoid fatigue during the MVC trials.

After collecting MVC data, subjects were asked to complete a series of ramp force trials. A ramp template was displayed as a thick red line on the computer screen. Each ramp force trial lasted 13 seconds long with the following sequential segments (Fig 1A): zero force in the 1st 2 seconds, an ascending ramp from zero to 20% MVC over 4 seconds, a 2-s plateau at 20% MVC, a descending ramp from 20%MVC to zero over 4 seconds, and finally one second of zero force. Subjects were asked to replicate this red ramp template to the best of their ability by pressing down with all four fingers simultaneously. The total force of four fingers was displayed on the screen. A full scale of the visual display was fixed at 40% MVC. Twelve practice trials were completed during the first session in order to familiarize the subjects with the task and negate any motor learning issues that might have confounded the data. Twenty seconds of rest were allotted to the subject after each practice trial to avoid fatigue. The second series of 12 ramp trials was saved to compare performance between ramp force generation and relaxation. The ramp series without TMS were always performed first to minimize the potential learning effect from TMS trials on multi-finger interactions.

Exp 2. TMS during force generation, maintenance and relaxation—The method and procedures of application of TMS was the same as described in previous studies (Li 2007; Li & Rymer 2011;Li et al. 2009). Focal TMS was performed with a figure-of-8-shaped stimulation coil (mean diameter of each wing 35 mm) connected to a Magstim BiStim² transcranial magnetic stimulator, consisting of two Magstim 200² units (Magstim Corp., UK). The intersection of the coils was placed tangentially to the scalp, approximately

positioned 2 cm to the left of the vertex (Cz), with the handle pointing backward and laterally at a 45° angle away from the midline. In this way, the current induced in the neural tissue was directed approximately perpendicular to the line of the central sulcus in a direction parallel to the mid-line between the two coils and therefore optimal for activating the corticospinal pathways transsynaptically (Brasil-Neto et al. 1992). In search of an optimal position for the finger flexors, the stimulus intensity was set at 60% of the stimulator output and the coil was moved over the scalp in steps of 1 cm. The optimal position was defined by eliciting the largest MEP in the finger flexors that was stable in three consecutive trials. Keeping the coil at the optimal location, the stimulation intensity was slowly decreased until the resting motor threshold (MT) was found. The MT was defined as the lowest stimulus capable of evoking at least 5 of 10 discernible motor evoked potentials (MEPs) with the amplitude of at least 50 μ V when subjects were at rest. The average MT was 42.7% in this study.

After MT was obtained, the following TMS protocols were used:

1. SICI (short-interval intracortical inhibition): a conditioning stimulus at 80% MT followed by a test stimulus at 120%MT with an interstimulus interval of 3ms;
2. LICI (long-interval intracortical inhibition): a conditioning stimulus at 110% MT followed by a test stimulus of 110% MT with an interstimulus interval at 100ms;
3. ICF (intracortical facilitation): a conditioning stimulus at 80%MT followed by a test stimulus of 120% MT with an interstimulus interval at 10ms
4. UNC (unconditioned): a test stimulus at 140%MT without a preceding conditioning stimulus.

Single- or paired-pulse TMS was given in the following 3 force conditions:

1. Up: TMS was triggered during the ascending ramp force production when the total force reached 10%MVC, i.e., half way up the ramp. Subjects were instructed to continue force production following the ramp template precisely, ignoring the TMS interruption;
2. Down: TMS was triggered during the descending ramp force relaxation when the total force reached 10%MVC, i.e., half way down the ramp. Similarly, subjects were instructed to continue force production following the ramp template precisely, ignoring the TMS interruption;
3. Static: TMS was randomly triggered during constant isometric force production. Subjects were also instructed to ignore the interruption.

These single- and pair-pulse TMS protocols were relatively standard. The absolute magnitudes of induced responses from current SICI, LICI, ICF or UNC protocols may vary, if the intensity of conditioning stimulus changed (Buccolieri et al. 2004; Maeda et al. 2002; Orth et al. 2003). These changes would not affect the purpose of the present study, which was to compare performance and responses among UP, Down, and Static conditions within subjects.

Delivery of single- or paired pulse TMS (SICI, LICI, ICF or UNC) was triggered when the total force reached 10%MVC during Up and Down conditions; while it was randomly triggered the Static condition. Any trial with visually detectable deviation of background total force from the target level during the Static condition was discarded. The trial was repeated. Each protocol of single- or paired-pulse TMS was given a block of 8 trials. Blocks of TMS were pseudo-randomized that a given protocol was delivered to all three force conditions in a randomly order, while the order of protocols was randomized. As in previous

studies, the coil was held by the experimenter. The hot spot was confirmed during and between blocks periodically. No movements were allowed at two upper limbs, shoulder joints and the head. To ensure no body and head movement during experiments, a cervico-thoracic brace (Lerman Minerva cervical orthosis, Trulife, Ireland) was used to stabilize the trunk, neck and head (Li et al. 2011).

Data Analysis

Data analysis was performed off-line using customized MatLab (MathWorks, MA) programs. The method for analysis of force variance profiles was well established (Kruger et al. 2007; Latash et al. 2002; Scholz et al. 2002; Shinohara et al. 2003; Shinohara et al. 2004). In this study, the force variance profiles were analyzed separately for force generation during the ascending ramp and force relaxation during the descending ramp.

Ramp force processing—Twelve trials were aligned by the nominal trial initiation. Average profiles of individual finger forces [$F_i(t)$] and of the total force [$F_{tot}(t)$] were computed (Fig 1B). Time profiles of the variance of the total force [$Var_Tot(t)$] and of the sum of variances of individual finger forces [$(Sum_Var(t))$] were computed over these trials were computed (Fig 1C). Variance values were further averaged over the ascending (force generation) and descending (force relaxation) ramp (Var_TotUP , Sum_VarUP , $Var_TotDown$, $Sum_VarDown$), respectively. Variance was computed over trials at comparable phases for further comparisons. The difference between the two variance indexes [$\Delta var(t) = Sum_Var(t) - Var_Tot(t)$] was computed to assess positive or negative covariations among individual finger forces. Note that a positive Δvar ($\Delta var > 0$) means negative covariations among finger forces, i.e., partial compensation of errors introduced by individual fingers in separate trials; while a negative Δvar ($\Delta var < 0$) indicates that positive covariations dominate, i.e., error amplification introduced by individual fingers. The variance difference (Δvar) was averaged over the ascending ($\Delta varUP$) and descending ramp ($\Delta varDown$), respectively.

TMS signal processing—The main dependent variables were motor evoked potential (MEP) and force response (F_{INC}) to TMS. Both MEP and F_{INC} magnitudes were compared among force production conditions. The methods for measuring magnitude of MEPs were the same as previously described (Li 2007; Li et al. 2004, 2009, 2011). Briefly, from the rectified, unfiltered EMG signals (FDS and EDC), the background EMG (EMG_{BG}) was defined as the mean EMG calculated from -100 ms to the moment of TMS application. The MEP onset was determined at the moment when it took the baseline EMG to increase by 2 SDs. The MEP magnitude was measured as the peak-to-peak difference which was normally within 50 ms after TMS application (Danion et al. 2003). MEP was measured for both FDS and EDC. Averaged across 8 trials for each TMS protocol, MEP magnitudes in response to paired-pulse TMS (SICI, LICI, ICF) were then normalized to the averaged MEP magnitude during single-pulse TMS (UNC) for each subject during Up, Down, and Static conditions, respectively. Similarly, the background force (F_{BG}) was calculated as the mean total force averaged over -100 ms to the moment of TMS application. The force response (F_{INC}) was defined as the difference between the peak force response and F_{BG} . Averaged F_{INC} during paired-pulse TMS was then normalized to the averaged F_{INC} during single-pulse TMS during Up, Down, and Static conditions.

FDS/EDC EMG ratio—The ratio of background EMG between FDS and EDC ($EMG_{BG_FDS}/EMG_{BG_EDC}$) was calculated to compare their co-contraction level during Up, Down, and Static conditions. Similarly, the FDS/EDC ratio was calculated using MEP magnitudes. MEPs for FDS and EDC were first averaged across different TMS protocols (SICI, LICI, ICF, UNC). The averaged MEPs were then used to calculate the FDS/EDC

ratio. Although MEP_EDC during TMS application to the FDS cortical area did not precisely represent excitability of the EDC cortical area, differences in FDS/EDC ratio in EMG and MEP could provide information of relative changes in excitability between FDS and EDC cortical areas during Up, Down, and Static conditions.

Statistics

Descriptive statistics were used. A repeated measure analysis of variance (ANOVA) was used to examine the effect of force generation and relaxation on ramp force variance profiles. The factors were VARIANCE (2 levels, Sum_Var and Var_Tot), and RAMP (2 levels, Up and Down). Student's t-tests were used to compare the variance difference during force generation and relaxation. A two-way ANOVA was used to examine the background force during different force conditions and TMS protocols with factors FORCE (3 levels, Up, Down, Static) and TMS (SICI, LICI, ICF, UNC).

Results

Force generation and relaxation during ramp force tasks without TMS

In the first experiment, subjects were asked to produce precisely controlled ascending ramp force (force generation), to maintain a constant force and then to produce precisely controlled descending ramp force (force relaxation). After a standardized 12 practice trials, subjects did not report that precisely controlled force generation and relaxation following a ramp template was a difficult task (Figure 1A). They did report subjectively, however, that controlled force relaxation was more difficult than controlled force generation. As shown in Figure 1 B, subjects had larger errors particularly during the first half of force relaxation, as compared to force generation. The difference was reflected in the variance profiles: sum of variance of individual finger forces (Sum_Var(t)) was greater than the variance of total force (Var_Tot(t)) during force generation (ascending ramp). In contrast, Sum_Var(t) was equal to or less than Var_Tot(t) during force relaxation (descending ramp). Averaged across subjects, a two-way ANOVA (VARIANCE $\times$ RAMP) revealed a main effect of RAMP ($F[1,8]=13.29$, $p=0.007$), and a main effect of VARIANCE $\times$ RAMP interaction ($F[1,8]=28.43$, $p=0.001$). Tukey Post-hoc tests showed that Sum_VarUp was not significantly different from Sum_VarDown, while Var_TotUp was significantly smaller than Var_TotDown ($p<0.001$). No main effect of VARIANCE was found.

The difference between Sum_Var and Var_Tot was defined as the variance difference (Δvar). On Figure 2A, Δvar was the difference between the first and second columns for force generation, and the third and fourth columns for force relaxation. As shown in Figure 2B, the averaged Δvar was positive (0.20) for force generation, and was negative (-0.33) for force relaxation. The difference was significant ($t_8=6.32$, $p<0.001$). These data indicated that there were negative covariations (i.e., $\Delta var>0$) among finger forces during force generation, but positive covariations (i.e., $\Delta var<0$) among finger forces during force relaxation. Given no difference in the sum of variances of finger forces between force generation and relaxation, errors introduced by fingers were partially compensated by negative covariations during force generation, while amplified by positive covariations during force relaxation. As a result, the performance (Var_Tot) was better during force generation than force relaxation (Var_TotUp < Var_TotDown).

Single- and paired-pulse TMS during force generation and relaxation

In the second experiment, single- (unconditioned, UNC) or paired-pulse (SICI, LICI, ICF) TMS were triggered when the total finger force reached its 10%MVC during force generation or relaxation, or randomly triggered when maintaining a constant force 10%MVC. The background force (F_{BG}) was not significantly different among TMS

protocols (SICI, LICI, ICF, UNC) and force conditions (Up, Down, Static) according to a 4×3 TMS×FORCE two-way ANOVA. On average, F_{BG} was 7.51N, 7.59N, and 7.55N for Up, Down, and Static force conditions, respectively. Similarly, when averaged for UP, Down, and Static force conditions, background EMG was not significantly different for FDS ($F[2,16]=3.34$, $p=0.061$) and EDC ($F[2,16]=1.59$, $p=0.234$).

Force increment (F_{INC}) in response to TMS had a unique pattern (Figure 3A). F_{INC} was greatest during Up, smallest during Down, both were significantly different from Static. Among TMS protocols, F_{INC} was significantly greater in UNC than in other conditions (SICI, LICI, and ICF) where no difference in F_{INC} was found. A 4×3 TMS×FORCE two-way ANOVA revealed main effects of TMS ($F[2,16]=101.3$, $p<0.001$), of FORCE ($F[3,24]=14.4$, $p<0.001$), and a significant TMS×FORCE interaction ($F[6,48]=6.7$, $p<0.001$). However, when normalized to F_{INC} in the corresponding UNC (i.e., divided by the fourth column in Figure 3A), the normalized F_{INC} was not different among Up, Down, and Static conditions (Figure 3B). But it was significantly greater in ICF than in SICI or LICI. A 3×3 ppTMS × FORCE two-way ANOVA showed a main effect of ppTMS ($F[2,16]=16.5$, $p<0.001$), but no main effect of FORCE or interactions.

A similar pattern of motor evoked potentials in FDS (MEP_FDS) was observed (Fig 4A). A 4×3 TMS × FORCE two-way ANOVA showed main effects of FORCE ($F[2,16]=12.6$, $p<0.001$), TMS ($F[3, 24]=23.3$, $p<0.001$), and a significant interaction ($F(6,48)=3.2$, $p=0.010$). According to post-hoc tests, the magnitudes of MEP_FDS were significantly smaller during Down than Up, or Static conditions, while the MEP_FDS magnitudes were significantly greater in UNC than in ICF. Both were significantly greater than in SICI and LICI, which were not significantly different from each other. When normalized to MEP_FDS in UNC, no difference in MEP_FDS among Up, Down, and Static was found. However, a 3×3 ppTMS×FORCE two-way ANOVA showed a main effect of ppTMS ($F[2,16]=44.3$, $p<0.001$) and a significant interaction ($F[4,32]=4.2$, $p=0.007$). Post-hoc Tukey tests showed MEP_FDS magnitudes were significantly greater in ICF than in SICI or LICI. To the contrary, the MEP_EDC magnitudes (Fig 4B) were not significantly different among Up, Down, and Static conditions. A 4×3 TMS×FORCE two-way ANOVA revealed no main effects of FORCE, or interaction, but a main effect of TMS ($F[3,24]=3.1$, $p=0.043$). Post-hoc Tukey tests revealed MEP_EDC magnitudes were greater in UNC than in LICI, no other difference was found.

The ratio between FDS and EDC was calculated using background EMG as well as MEP (Fig 5). A RATIO × FORCE two-way ANOVA revealed main effects of RATIO ($F[1,8]=13.9$, $p=0.006$), FORCE ($F[2,16]=7.3$, $p=0.006$), and a significant interaction ($F[2,16]=9.1$, $p=0.002$). Post-hoc Tukey tests showed that the FDS/EDC ratio was significantly greater during TMS applications than during background force production; the ratio was significantly smaller during Down than during Up or Static; and the ratio was not significantly different between Up and Static during both background force production and TMS applications.

Discussion

Possible mechanisms for voluntary finger force generation and relaxation

The current study directly compared responses to single- and paired-pulse TMS during multi-finger force generation, maintenance, and relaxation. Changes in responses (MEP and force) to single-pulse TMS reflects excitability of the entire corticospinal tract and possibly other descending tracts, including spinal mechanisms (Paus et al. 1997) during finger force production. Single-pulse TMS was triggered when the same target force (10%MVC) was reached during force generation and relaxation. Background force was not significantly

different between generation (average: 7.51N), maintenance (7.55N) and relaxation (7.59N). No difference in background EMG was found either. Both MEP and force responses were greater during force generation than maintenance or relaxation. These results indicated greater excitability during finger force generation than during force relaxation. Consistent with these findings, Spraker et al. in a recent fMRI study (Spraker et al. 2009) reported greater activation in M1 during force generation than force relaxation, while no difference was found in premotor cortex, SMA and pre-SMA areas.

The greater corticospinal excitability during force generation was not likely attributable to difference in intracortical mechanisms in the motor cortex network. Finger force and finger flexor EMG responses during paired-pulse TMS, when normalized to their corresponding values during unconditioned, single-pulse TMS, showed no difference in SICI, LICI, or ICF. The findings suggest that intracortical facilitation or inhibition within the primary cortex (M1) or the motor cortex network was proportional to its overall corticospinal excitability, thus not responsible for difference in force generation, maintenance or relaxation.

The greater MEPs during force generation could be attributed to spinal mechanisms as mentioned earlier (Paus et al. 1997). Kimura et al. (Kimura et al. 2003) compared MEPs of elbow flexors between the force generation and relaxation ramps during rhythmic elbow flexion at different frequencies. Similar to the present findings, the authors found greater MEPs during the force generation than relaxation phase. They ascribed the difference to hysteresis of corticospinal excitability. However, the corticospinal hysteresis during rhythmic movement may not be applicable to account for the difference between discrete finger force generation and relaxation in the present study, since rhythmic and discrete movements involve different cortical areas and require separate neurophysiological and theoretical treatment (Schaal et al. 2004).

The smaller MEPs during force relaxation could be resulted from greater overall inhibition to the finger flexors area. A recent fMRI study (Spraker et al. 2009) reported greater activation in contralateral dorsal lateral prefrontal cortex (DLPFC) and greater deactivation in bilateral anterior cingulate cortex (ACC) during discrete force relaxation. Furthermore, the FDS/EDC ratio (i.e., co-contraction) in MEP was greater during force generation as compared force relaxation in the present study. However, the FDS/EDC ratio in baseline pre-TMS EMG (Figure 5) was not significantly different among force generation, maintenance and force relaxation. These results suggest relaxation of finger flexion force was likely due to inhibition from higher centers to the M1 finger flexor area, rather than increased co-contraction, or increased antagonist (i.e., EDC) activation. However, there is a limitation of the study that mechanical or electrical (MEP) responses to TMS strongly depend on the activity and excitability of motoneurons and thus do not directly reflect the state of the corticospinal influences during isometric force generation as analyzed in the study.

Multi-finger interactions during finger force generation and force relaxation

Subjects demonstrated more variable performance during force relaxation as compared to force generation. Errors introduced by a finger force were partially compensated by other finger forces during force generation (i.e., multi-finger synergy), but amplified during force relaxation (i.e., no multi-finger synergy) (Figs 1 and 2). In a similar force generation and relaxation task involving pinch grip only by right thumb and middle finger, grip force error was the same between force generation and relaxation (Spraker et al. 2009). As discussed in the previous study (Spraker et al. 2009), there was no difference in complexity or difficulty of following an increasing vs. decreasing ramp template. Complexity of the task increased when the number of digits participated in the task increased, arguably resulting in more variable performance. Shim et al. reported similar findings of more variable performance

during force relaxation when involving all five digits (four fingers and thumb) (Shim et al. 2005).

The finding of error amplification during force relaxation, in combination with TMS and fMRI findings of overall inhibition to the M1 from higher centers during force relaxation, suggests that multi-finger interactions are likely controlled beyond the primary motor cortex. There exists corticocortical connection from the prefrontal cortex to the motor cortex (Lu et al. 1994; Luppino et al. 1993; Rizzolatti et al. 1998). Increased activation in DLPFC has been consistently associated with response inhibition (Garavan et al. 2002; Garavan et al. 1999; Kawashima et al. 1996; Nakata et al. 2008; Watanabe et al. 2002). Increased activation in DLPFC during force relaxation could impose a general inhibition to the motor system, resulting in decreased M1 excitability with proportionally decreased intracortical inhibitory and facilitatory activities. In addition, increased deactivation in ACC is associated with decreased ability of error detection (Garavan et al. 2002) and less selective attention (Lane et al. 1998) during force relaxation. These findings could explain error amplification among finger forces during force relaxation as compared to error compensation during force generation. However, such comparisons of multi-finger interactions with fMRI imaging would provide definitive evidence.

On the other hand, organization of synergies are possibly related to the method of control with referent configurations (Latash 2010). It has recently been shown that corticospinal facilitation shifts the referent position (configuration) at which muscles are activated (Raptis et al. 2010; Sangani et al. 2011). It is also known that it takes more time to relax than to activate muscles. In the present study, the rates of the ascending and descending ramps were equal. Thus, to compensate for the greater relaxation time, the rate of decrease in the referent position of fingers during relaxation ramp should be greater than during the ascending ramp, which explains why corticospinal facilitation in the former case was smaller, even though the force levels were the same. In other words, there is a shift in the referent configuration during force relaxation, as compared to force generation. In such a referent configuration shift during force relaxation where a discrete force production is to be stopped, the “bad” variance at the level of individual fingers is likely to increase (cf. Skm et al. 2010), resulting in error amplification during force relaxation.

In conclusion, the present study clearly indicates that 1) errors from a finger are partially compensated by other fingers during force generation, but are amplified during force relaxation; 2) corticospinal excitability is greater during force generation compared with force relaxation; and 3) there is no difference in intracortical facilitation and inhibition between force generation and relaxation. These results suggest that force relaxation is not just a withdrawal from activation, and multi-finger interactions are likely controlled beyond the primary motor cortex.

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Figure 1.

Panel A: a ramp force template and a trace (dotted line) of the total force averaged from 12 trials from a representative subject; Panel B: a plot of 12 individual trials and their average (solid line); Panel C: sum of variance of individual finger forces (Sum_Var) and variance of total force (Var_Tot). Note that Sum_var is greater than Var_Tot during force generation, but similar or even smaller during force relaxation.

Figure 2.

Upper panel (A): Mean and standard errors of sum of variance of individual finger forces (Sum_Var) and variance of total force (Var_Tot) during force generation (Up) and force relaxation (Down). The difference between Sum_Var and Var_Tot (Δvar) is plotted in the lower panel (B). There is error compensation ($\Delta\text{var}>0$) during force generation, but error amplification ($\Delta\text{var}<0$) during force relaxation.

Figure 3.

A: Mean and standard errors of TMS-induced force responses (F_{INC}) during force generation (Up), maintenance (Static) and force relaxation (Down). SICI: short-interval intracortical inhibition; LICI: long-interval intracortical inhibition; ICF: intracortical facilitation; UNC: unconditioned. UNC and SICI, LICI, ICF all showed similar pattern: greater during force generation than force relaxation. When normalized to UNC, SICI, LICI, and ICF showed no significant difference among force generation, maintenance and relaxation (B), indicating proportional intracortical activities among these force production conditions.

Figure 4. Mean and standard errors of TMS-induced EMG responses in the finger flexors (A) and the finger extensors (B) during force generation (Up), maintenance (Static) and force relaxation (Down).

FDS/EDC ratio

Figure 5. Mean and standard errors of FDS/EDC ratio during force generation (UP), maintenance (Static), and force relaxation (Down).