J Neurophysiol 107: 1522–1529, 2012.
First published December 7, 2011; doi:10.1152/jn.00786.2011.

Task-dependent changes of motor cortical network excitability during precision grip compared to isolated finger contraction

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[1]*Université Paris 5 René Descartes, Institut de Psychologie, Boulogne-Billancourt, France;* [2]*Brain and Movement Laboratory, Department of Electrical Engineering, Technical University of Denmark, Lyngby, Denmark; and* [3]*Université Lille-Nord de France, Laboratoire de Neuroscience Fonctionnelle et Pathologies, Hôpital Roger Salengro, CHRU Lille, Lille and* [4]*Université Lille-Nord de France, ULCO, Calais, France*

Submitted 25 August 2011; accepted in final form 5 December 2011

Kouchtir-Devanne N, Capaday C, Cassim F, Derambure P, Devanne H. Task-dependent changes of motor cortical network excitability during precision grip compared to isolated finger contraction. *J Neurophysiol* 107: 1522–1529, 2012. First published December 7, 2011; doi:10.1152/jn.00786.2011.—The purpose of this study was to determine whether task-dependent differences in corticospinal pathway excitability occur in going from isolated contractions of the index finger to its coordinated activity with the thumb. Focal transcranial magnetic stimulation (TMS) was used to measure input-output (I/O) curves—a measure of corticospinal pathway excitability—of the contralateral first dorsal interosseus (FDI) muscle in 21 healthy subjects performing two isometric motor tasks: index abduction and precision grip. The level of FDI electromyographic (EMG) activity was kept constant across tasks. The amplitude of the FDI motor evoked potentials (MEPs) and the duration of FDI silent period (SP) were plotted against TMS stimulus intensity and fitted, respectively, to a Boltzmann sigmoidal function. The plateau level of the FDI MEP amplitude I/O curve increased by an average of 40% during the precision grip compared with index abduction. Likewise, the steepness of the curve, as measured by the value of the maximum slope, increased by nearly 70%. By contrast, all I/O curve parameters [plateau, stimulus intensity required to obtain 50% of maximum response (S_{50}), and slope] of SP duration were similar between the two tasks. Short- and long-latency intracortical inhibitions (SICI and LICI, respectively) were also measured in each task. Both measures of inhibition decreased during precision grip compared with the isolated contraction. The results demonstrate that the motor cortical circuits controlling index and thumb muscles become functionally coupled when the muscles are used synergistically and this may be due, at least in part, to a decrease of intracortical inhibition and an increase of recurrent excitation.

transcranial magnetic stimulation; motor task dependence; primary motor cortex; intracortical inhibition

THERE IS NOW AMPLE EVIDENCE from neurophysiological studies in humans and animals that the excitability of neural networks involved in motor control is modulated in a task-dependent manner. For example, at the spinal level, the gain of the human H-reflex decreases in going from standing to walking and further during running (Capaday and Stein 1986, 1987a; Schneider et al. 2000). Reciprocal inhibition of the ankle extensors is more powerful during the swing phase of walking than in other motor tasks (Lavoie et al. 1997). At the cortical level, corticomotoneurons have been shown to be more active during a precision grip task than during a power grip in monkeys (Buys et al. 1986; Muir and Lemon 1983). Such changes of neural circuit excitability have been suggested to be adaptive to the functional requirements of the motor task.

The development of transcranial magnetic stimulation (TMS) has allowed the study of task-dependent modulation of motor cortical network excitability noninvasively in humans (see, e.g., Capaday et al. 1999; Devanne et al. 2002; Schieppati et al. 1996; Stinear and Byblow 2005). Datta et al. (1989) were among the first to explore possible changes in corticospinal excitability using TMS. They reported an increase of first dorsal interosseus (FDI) motor evoked potential (MEP) amplitude during isolated index abduction compared with a power grip. However, their findings were contested by subsequent studies (Flament et al. 1993; Hasegawa et al. 2001; Huesler et al. 1998). In particular, Flament et al. (1993) reported the opposite, i.e., the excitability of the corticospinal pathway to the FDI was lower in the relatively isolated contraction involved in finger abduction compared with tasks that involved coactivation of the FDI with thumb muscles, such as in the power grip, the pincer grip, and the rotational grip. Whether there are indeed differences in motor cortical excitability between these tasks and, more importantly, the neural mechanisms underlying any such differences remains unresolved. The increased excitability of the corticospinal pathway to the FDI during coactivation with thumb muscles reported by Flament et al. (1993) bears a striking resemblance to the results of the study of cortical control of arm pointing by Devanne et al. (2002). They demonstrated that the excitability of the corticospinal pathway to the extensor carpi radialis (ECR) was markedly increased when it was coactivated with the anterior deltoid (AD) during pointing, compared with an isolated contraction of the ECR. In other words, activation of a proximal shoulder muscle (AD) strongly facilitated the MEPs of the more distal ECR when they were coactive during pointing.

A task-dependent change of corticospinal pathway excitability, as determined by changes in MEP amplitude, should be associated with changes in the ratio of facilitation and inhibition. For example, increased excitability may be the result of decreased intracortical inhibition or increased intracortical facilitation (ICF). Indeed, Devanne et al. (2002) observed that the enhanced ECR MEPs during pointing were associated with decreased short-latency intracortical inhibition (SICI) tested at the ECR site. By contrast, no changes in ICF were found. To our knowledge, such measurements of intracortical facilitation

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and inhibition that may accompany potential task-dependent changes in corticospinal pathway excitability to digit muscles have not been made. Consequently, we thought of using the method of input-output (I/O) measurement of corticospinal pathway excitability (Devanne et al. 1997) to resolve the issue of task-dependent changes and, in the event, probe the neural mechanisms involved by measuring changes of intracortical facilitation and inhibition.

METHODS

Ethical approval and subjects. Twenty-one healthy subjects (11 men, 10 women) aged from 20 to 50 yr (mean ± SD age 35.8 ± 9.4 yr) participated in the study after giving their written informed consent. They did not take any medication and did not have any neurological or psychiatric disease. The study conformed to the Declaration of Helsinki and was approved by the local ethics committee (the "Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale") in Lille, France.

General outline of the study. The aim of our study was to compare cortical excitability during isometric index abduction with a precision thumb-index grip task at similar levels of FDI EMG activity. In the index abduction task, subjects were asked to maintain isometric index abduction against a wooden block at 10% of maximal voluntary contraction (MVC). The second task consisted of an isometric precision grip between index finger and thumb at 10% of MVC in the FDI muscle. The subjects were instructed to maintain a cylinder vertically oriented. The cylinder had a diameter of 6 cm and a length of 7 cm and weighed ~100 g. We measured I/O curves of FDI MEPs vs. TMS intensity (Devanne et al. 1997) to determine changes of global corticospinal excitability, if any. We also measured changes of SICI, long-latency intracortical inhibition (LICI) and ICF, as well as silent period (SP) duration in the two tasks. Details of these experimental methods and the data analysis procedures follow.

Electromyographic recordings. Subjects sat in a comfortable armchair. Their preferred forearm rested on a height-adjustable table placed near them with the height adjusted to each subject's comfort. Ag-AgCl surface electrodes were used to record the electromyographic (EMG) activity of the FDI muscle of the dominant hand with a belly-tendon montage. In some subjects, EMG activity from three other muscles was recorded: abductor pollicis brevis (APB), ECR, and flexor carpi radialis (FCR). EMG signals were amplified (1000×), high-passed at 10 Hz, and low-passed at 1,000 Hz (Grass Technologies, West Warwick, RI) prior to sampling at 2 kHz with a 1401MicroMKII device (Cambridge Electronic Design, Cambridge, UK). The data were stored on a computer for subsequent off-line analysis with customized Signal software (Cambridge Electronic Design). Subjects' digits and wrist were stabilized between homemade wooden blocks to restrict movement to abduction of the index finger. Digits III, IV, and V were tied together. Subjects first produced maximal voluntary index abduction in three successive trials. A 1401+ device (Cambridge Electronic Device) was used in parallel with customized Spike2 software (Cambridge Electronic Design) to record and display the root mean square (RMS) EMG level of the low-passed (100 Hz) FDI signal as a percentage of MVC EMG.

Transcranial magnetic stimulation. TMS was delivered with a 9.5-cm external diameter figure-of-eight focal coil connected to two Magstim 200 stimulators via a Bistim module (Magstim, Whitland, UK). Stimulation was applied over the optimal scalp point for the FDI of the dominant hand, i.e., the site that yielded the strongest FDI MEPs at a given suprathreshold intensity. This point was determined by moving the coil over the hand motor area while the subject relaxed his/her arm muscles. To ensure constant coil positioning throughout the series, the FDI's optimal scalp point was marked on a swimming cap worn by the subject. The coil was held tangentially to the scalp, with the handle pointing backward and laterally (at a 45° angle from the midline). We then measured the FDI's resting motor threshold (RMT_{FDI}), defined as the lowest possible stimulus intensity capable of inducing MEPs >50 μV in at least 5 out of 10 trials, and FDI's active motor threshold (AMT_{FDI}), defined as the minimum stimulus intensity to produce MEPs of ~200 μV in 5 out of 10 trials during an isometric FDI contraction at 10% of MVC. During the I/O series, the intensity of the magnetic stimulus was increased in steps of 3–5% of the stimulator output, from the subthreshold intensity (3% beneath AMT_{FDI}) up until the maximal output intensity (100%). Eight stimuli were delivered at each intensity, with a randomly selected interstimulus interval (ISI) of between 4 and 6 s.

SICI and ICF. SICI and ICF were measured according to the paired-pulses method described by Kujirai et al. (1993) during each task with FDI muscle activated at 10% of MVC. The intensity of the conditioning stimulus was 90% of AMT_{FDI}, and the test stimulus was set separately in each task to evoke a MEP of 1 mV in the FDI. Two ISIs were tested: 3 ms and 11 ms. During the series, eight conditioned responses were recorded in random order for each interval and eight unconditioned test stimuli were also delivered pseudorandomly throughout the block. For each ISI, the average conditioned peak-to-peak MEP amplitude was measured and expressed as a percentage of the unconditioned MEP.

LICI. LICI was measured while the FDI muscle was activated at 10% in each of the two tasks. Two suprathreshold stimuli were delivered with an ISI of 100 ms. Stimulus intensity was set separately in each task so that it evoked on its own an MEP ~1 mV in amplitude. On average across subjects, stimulus intensity was 44.6 ± 2.8% during index abduction and 44.4 ± 2.9% in precision grip. Eight pairs of stimuli and eight unconditioned stimuli were delivered pseudorandomly. The average conditioned peak-to-peak MEP amplitude was measured and expressed as a percentage of the unconditioned MEP.

Data analysis. Signals were averaged off-line over a 250-ms time window (which included the 50-ms period prior to stimulation) for each stimulus intensity. We measured peak-to-peak amplitude of motor responses and duration of SP. An algorithm was used to measure SP duration from the start of the MEP to the return of EMG activity above the mean prestimulus level measured during a 50-ms period prior to the magnetic pulse. The MEP amplitude and SP duration were plotted against the stimulus intensity. We used the Levenberg-Marquard nonlinear least-mean-squares algorithm (Press et al. 1986) to fit the data points to the Boltzmann equation. The equation relates MEP amplitude to stimulus intensity (S) as follows:

$$\mathrm{MEP}(S) = y_0 + \frac{\mathrm{MEP}_{\mathrm{MAX}}}{1 + e^{(S_{50}-S)/k}}$$

This equation has four parameters: MEP_{MAX} is the maximum value or the plateau of the curve, S_{50} is the stimulus intensity required to obtain 50% of the maximum response, and the reciprocal of the parameter k (i.e., $1/k$) is directly proportional to the maximum slope of the curve, which occurs at S_{50}. Note that two curves with the same slope parameter k but different plateau values will rise at different rates. For example, the maximum slope (rate of change) occurs at S_{50} and has a value of $MEP_{MAX}/4k$. Here we used the value of the maximum slope as a measure of the steepness of the sigmoid curve defined by the Boltzmann equation. The fourth parameter (y_0) is the floor of the curve. A similar function was used to fit the relation between the SP duration (instead of MEP amplitude) and stimulus intensity. In this latter case, the fourth parameter y_0 was constrained to zero.

Statistical analysis. Three different methods were used to assess the influence of the task on the plateau value, slope, and S_{50} values of the I/O curves (see also Capaday et al. 1999; Devanne et al. 2002). The first two methods were used to determine whether or not there was a difference between the tasks for a given subject. The simplest method is based on the standard error of estimate and determines (with a paired t-test) whether or not the best-fit parameters differ between tasks. A more general approach, which considers the data sets as a whole, uses an

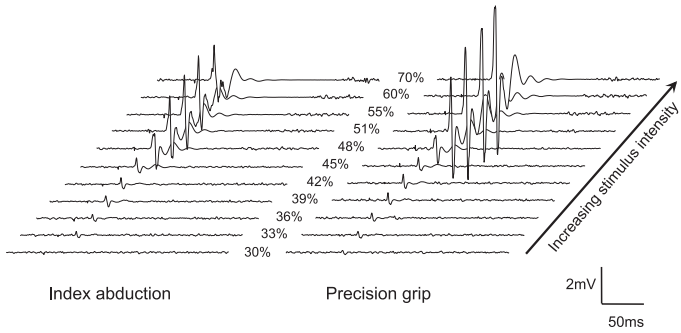

Fig. 1. Recordings of first dorsal interosseus (FDI) motor evoked potentials (MEPs) evoked by transcranial magnetic stimulation (TMS) at increasing stimulus intensities during index abduction and precision grip in 1 subject at the same level of FDI EMG background (41.7 ± 3.6 μV and 43.6 ± 4.2 μV for abduction and precision grip, respectively; $P = 0.838$).

F-test to determine whether or not fitting a curve to each data set significantly improves the total variance accounted for compared with fitting a single curve to all the data sets. This is formally equivalent to a multiple analysis of variance. The third method was a between-subjects comparison (i.e., across all repetitions of the experiment) for each estimated parameter using a general linear model for repeated measures (RM) with task condition (2 levels) as repeated within-subject factor and sex (female and male) as between-subjects factor to examine the task-related effects and possible sex differences. Comparison of the S_{50} parameter between MEP amplitude vs. SP I/O curves was made with an unpaired *t*-test. Statistical analysis was performed with GraphPad Prism (GraphPad Software, La Jolla, CA), and SPSS software v.15 (SPSS, Chicago, IL).

Background EMG levels were compared between tasks with a Friedman RM analysis of variance (ANOVA) on ranks. For the SICI/ICF experiment, the effect of ISI and task condition was examined with a two-way RM ANOVA with ISI (2 levels) and task condition (2 levels) as repeated factors (SPSS general linear model). In the case of a significant effect of ISI, a paired *t*-test was used to compare conditioned response at each ISI with unconditioned control MEP. The influence of task condition on LICI and the difference between unconditioned and conditioned response size in LICI series were assessed with a paired *t*-test. To reduce interindividual variability, the mean size of the conditioned MEP for each ISI in SICI/ICF series and in LICI series was expressed as a percentage of the mean size of the unconditioned MEP and the results reported as means ± SE. For all statistical tests, the results were considered to be statistically significant when $P < 0.05$. In RESULTS, values are expressed as means ± SE.

RESULTS

MEP size vs. stimulus intensity. All but one subject were able to produce the same level of tonic voluntary EMG activity in the FDI in the two tasks. One subject was excluded from off-line analysis because the levels of prestimulus EMG recorded from the target muscle differed in the two experimental conditions. Figure 1 shows typical recordings of FDI motor responses evoked by increasing stimulus intensities during index abduction and precision grip. The R^2 value of the fitting with a Boltzmann sigmoidal equation, which can be seen as a fraction of the total variance, ranged between 0.895 and 0.997 (average values: 0.962 ± 0.0057 for abduction and 0.973 ± 0.0048 for precision grip; $P = 0.102$). In most of the subjects, MEPs were of higher amplitude during the precision grip than during index abduction at stronger stimulus intensities (Fig. 2, *A* and *B*). A within-subject comparison of the I/O parameters revealed that the plateau value was significantly greater during the precision grip than during index abduction in 16 of 20 subjects; there was no significant task difference in the 4 remaining subjects. On average across subjects, the plateau value was significantly higher during the precision grip than during index finger abduction (3.96 ± 0.35 mV and 5.53 ± 0.35 mV, respectively; $P < 0.001$) (Fig. 3). The maximal slope values averaged across subjects were 0.40 ± 0.08 in the abduction task and 0.67 ± 0.12 in the precision grip task, an increase of nearly 70%, the difference being highly significant (Wilcoxon signed rank test; $P = 0.006$) (Fig. 3). In contrast, as shown in Fig. 3, the S_{50} parameter was not statistically different ($P = 0.343$) between abduction (52.54 ± 2.12%) and precision grip (51.65 ± 2.30%), although some individual differences were observed in seven subjects. It is important to note that while the S_{50} parameter may be the same, the size of the MEP obtained at that stimulus intensity is not, as can be seen in Fig. 2. For all three parameters, there was no sex difference or interaction between sex and task condition. In summary, the I/O curves measured during the precision grip rose to a higher plateau value and at a faster rate compared with those measured during index finger abduction.

Silent period duration vs. stimulus intensity. The duration of the SP was measured while subjects maintained an isometric FDI contraction of 10% of MVC in both tasks. The SP duration increased sigmoidally (Fig. 2, *C* and *D*) with TMS intensity, as did MEP amplitude. The R^2 value of the fitting with a Boltzmann sigmoidal equation ranged between 0.885 and 0.994 (average values: 0.958 ± 0.0061 for abduction and 0.961 ± 0.0072 for precision grip; $P = 0.985$). However, in contrast with MEP I/O curves, the plateau of the SP I/O curves was not significantly different between tasks (abduction: 191.71 ± 4.77 ms, precision grip: 190.00 ± 7.20 ms; $P = 0.180$). Likewise,

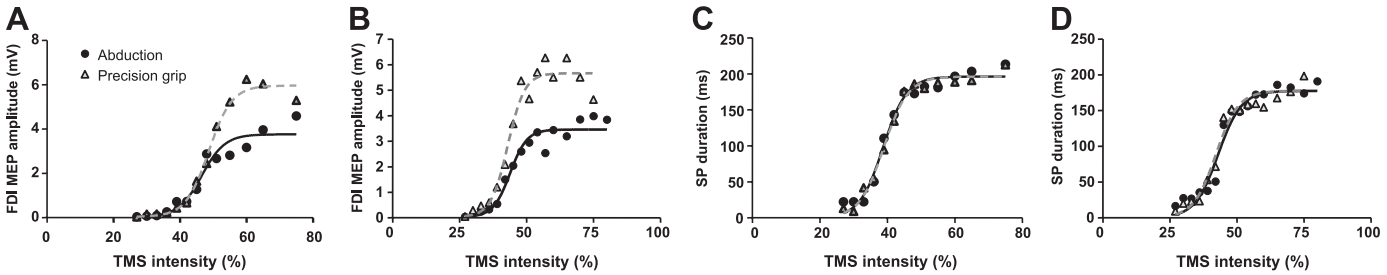

Fig. 2. Input-output (I/O) curves of MEP amplitude (*A* and *B*) and silent period (SP) duration (*C* and *D*) obtained in 2 subjects during index abduction (black circles, solid lines) and precision grip (gray triangles, dashed lines). In *subject 1* (*A* and *C*) the background FDI EMG was 25.8 ± 2.9 μV during abduction and 30.4 ± 2.4 μV during precision grip ($P = 0.846$). In *subject 2* (*B* and *D*) the background EMG of FDI was 46.6 ± 3.0 μV during abduction and 50.8 ± 3.5 μV during precision grip ($P = 0.451$). For *subject 1*, plateau value was greater during precision grip than during abduction.

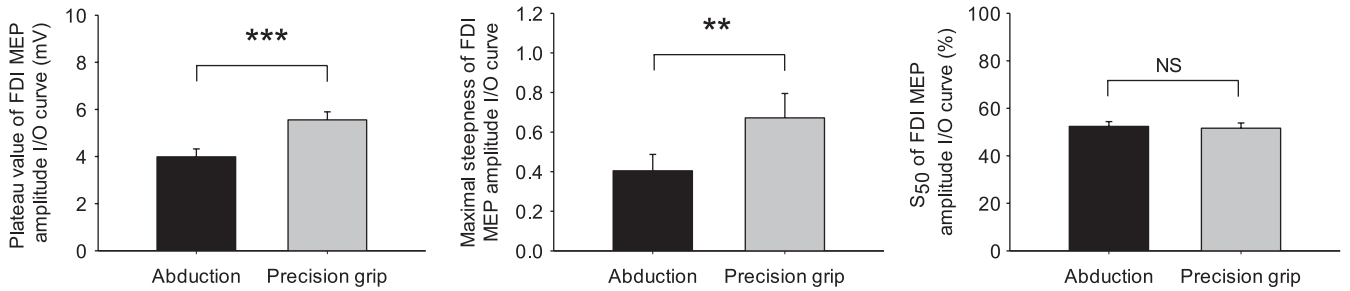

Fig. 3. Parameters of I/O curves of FDI MEP amplitude: plateau value (*left*), slope parameter (*center*), and stimulus intensity required to obtain 50% of maximum response (S_{50}; *right*) in abduction task (black bars) and precision grip (gray bars). Each bar corresponds to an average (±SE) obtained across all subjects. **Significant difference at $P < 0.01$; ***significant difference at $P < 0.001$. NS, not significant.

the maximum slope and S_{50} parameters were also not statistically different between the tasks (Fig. 2, *C* and *D*).

Comparison of MEP amplitude and SP duration I/O curves. In most subjects for a given task the MEP amplitude I/O curve was shifted to the right of the SP duration I/O curve (Fig. 4*A*). That is, the S_{50} parameter was greater for the MEP amplitude I/O curve than for the SP duration I/O curve. Additionally, the SP I/O curve most often reached its plateau value at much lower TMS intensities than the MEP I/O curve. Consequently, during abduction, the S_{50} value was significantly lower for the SP than the MEP I/O curve (45.81 ± 1.89% vs. 52.54 ± 2.12%, respectively; $P < 0.001$), indicating a shift toward lower stimulus intensities (Fig. 4*B*). Similarly, the S_{50} parameter of the SP I/O curve was lower than that of the MEP size I/O curve (45.13 ± 1.90% vs. 51.65 ± 2.30%, respectively; $P < 0.001$) during thumb-index precision grip (Fig. 4*B*).

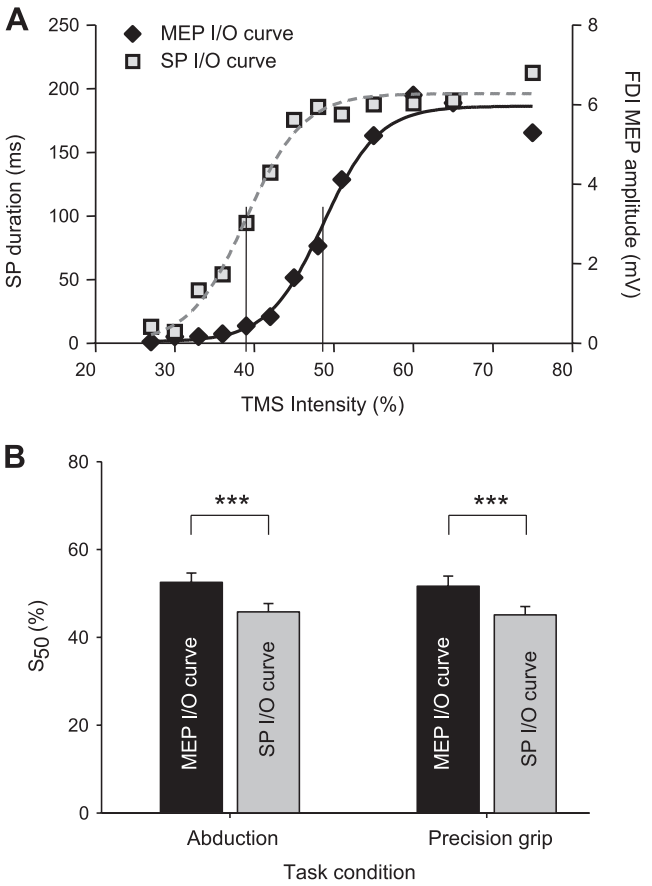

Fig. 4. Comparison of S_{50} parameter between MEP and SP I/O curves. In *A*, MEP I/O (black diamonds, solid line) and SP I/O (gray square, dashed line) curves were obtained in 1 subject during precision grip. Vertical lines indicate S_{50} value of MEP I/O and SP I/O curves. Average values across all subjects are represented in *B*. In each task, the S_{50} parameter was significantly lower for the SP I/O curve than for the MEP I/O curve. ***Significant difference at $P < 0.001$.

SICI and ICF. SICI and ICF were measured in 19 subjects. As in the I/O experiment, there was no significant difference of EMG background level between the two tasks. The two-way RM ANOVA indicated that there was a significant effect of ISI ($P = 0.042$) but not of the task condition ($P = 0.709$). During index abduction, SICI of FDI MEPs was significant [i.e., the conditioned MEP was 80.95 ± 7.90% of the unconditioned (control) MEP; $P = 0.04$]. Despite some trends toward facilitation at ISI of 11 ms (124.72 ± 13.19%), the conditioned MEPs were not significantly different from unconditioned MEP ($P = 0.123$) (Fig. 5). During the precision grip, there was no statistical difference between unconditioned and conditioned MEPs, regardless of ISI (Fig. 5).

LICI. LICI was measured in eight subjects during index finger abduction and precision grip. The EMG level was not significantly different between the two tasks. In seven subjects, the conditioned FDI MEP amplitude was reduced by an average of 57.51 ± 8.00% (Fig. 6) during index abduction, demonstrating the presence of robust LICI ($P = 0.042$). By contrast, LICI was only observed in one subject (S7) during the precision grip, and the conditioned MEP was even facilitated in five subjects (S1, S2, S3, S5, S6) during the same task (Fig. 6). On average across subjects, LICI was significantly lower in precision grip compared with abduction (119.36 ± 9.49% vs. 65.61 ± 10.66% of control, respectively; $P = 0.006$). Importantly, across all subjects during precision grip the conditioned MEP was in fact not significantly different from the unconditioned (control) MEP ($P = 0.084$). There was thus a strong reduction in the efficacy of LICI during the precision grip.

DISCUSSION

The purpose of this study was to resolve the issue of task-dependent changes of corticospinal pathway excitability using the method of I/O measurements. We have shown that the plateau (or maximum MEP) level of FDI I/O curves was on average 40% greater during the precision grip task compared with the simple finger abduction task, for matched levels of ongoing EMG activity. This was accompanied by an increased recruitment gain as measured by the maximum slope value of the I/O curves. Consequently, we probed the neural mechanisms involved by measuring changes of intracortical facilitation and inhibition. The substantial task-dependent changes of

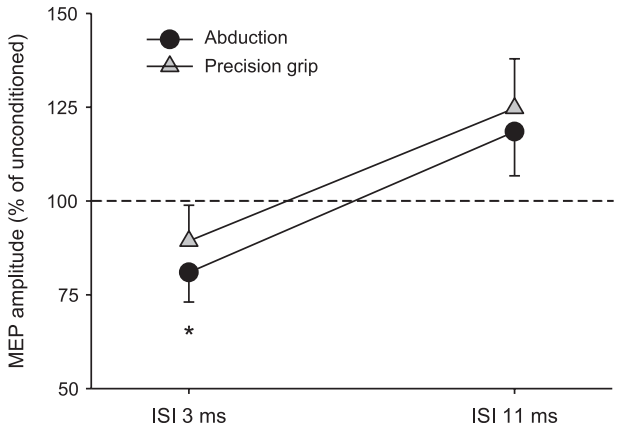

Fig. 5. Short-latency intracortical inhibition and intracortical facilitation during index abduction (black circles) and precision grip (gray triangles). Each symbol corresponds to the average ratio of conditioned to unconditioned MEP measured across all subjects at interstimulus intervals (ISIs) of 3 ms and 11 ms. *Significant difference ($P < 0.05$) between conditioned and unconditioned MEPs.

the FDI I/O curves were accompanied by a small reduction of SICI and a marked decrease of LICI. No changes in ICF were observed. Taken together the results demonstrate that the excitability of the corticospinal pathway to the FDI was greater during the precision grip than during simple index abduction and that this was accompanied by a reduction in the efficacy of intracortical inhibition as measured by SICI and LICI protocols. Our results corroborate those of Flament et al. (1993) and Hasegawa et al. (2001), who reported larger FDI MEPs during more complex tasks requiring muscle coordination, such as the rotation grip and pincer grip, compared with simple index abduction. The I/O method thus clearly reveals any task-dependent change and ipso facto is effective at disambiguating contradictory findings. The increased plateau of the MEP I/O curves represents recruitment of a greater proportion of α-motoneurons, over the same range of stimulus intensities. This scaling is a direct sign of increased corticospinal pathway excitability, as elaborated further below. The increased plateau value was accompanied by an increased steepness of the I/O curves, as measured by the maximum slope value, without change of the S_{50} parameter. The steepness of the I/O curve reflects the recruitment gain of the corticospinal pathway, whereas the S_{50} parameter is related to the stimulus threshold (Devanne et al. 1997).

In the discussion that follows we begin by addressing the functional significance of the enhancement (scaling) of the FDI I/O curve during the precision grip. We then consider the neural mechanisms that may underlie this scaling and the accompanying increased recruitment gain. Finally, we make the point that measurements of SP duration do not fully reflect the strength of intracortical inhibition and are thus inadequate to reveal task-dependent changes.

Functional significance. Holding an object between the thumb and index finger requires coordinated control of the force exerted by each digit on the object. While there is a controversy as to whether the finger muscles are controlled by a common descending drive from the motor cortex (Hepp-Reymond and Maier 1996), there is no question that at the functional (task) level the thumb and index are controlled synergistically (Johansson 1996). In the present static task, holding a cylinder vertically between thumb and index finger, the forces exerted by each digit must be equal and oppositely directed. Therefore, the descending corticospinal drive to the respective α-motoneuron pools must be, by whatever mechanism, appropriately balanced for the requisite mechanical effect. Inevitably, therefore, the task requires a functional coupling between the thumb and index finger muscles. We suggest that this is reflected by the increase of the FDI I/O curve plateau that we have observed when the thumb and index finger are functionally coupled in the precision grip. The TMS stimulus was applied at the same operationally defined optimal FDI site and with the same range of stimulus intensities in both tasks. The activated cortical area and subthreshold stimulus spread are therefore the same in the two tasks, yet the FDI I/O curve plateau was markedly elevated when the thumb and index finger were used together in the precision grip, while the FDI background EMG was equal to that during its isolated contraction. Clearly, the enhanced FDI MEPs during the precision grip must reflect either a change of excitability of corticospinal neurons innervating the FDI α-motoneurons or the activation of a task-specific group of corticospinal neurons. The latter possibility implies that the hypothetical task-related group has access to a greater proportion of the FDI α-motoneuron pool, explaining the higher plateau level observed in the precision grip. The current evidence is that, at least for corticomotoneurons, their intraspinal branches innervate most if not all the α-motoneurons of a motor pool (Porter and Lemon 1993). Thus, while the engagement of a task-related group of corticospinal neurons during the precision grip cannot be discounted, we suggest that the main mechanism is an increase

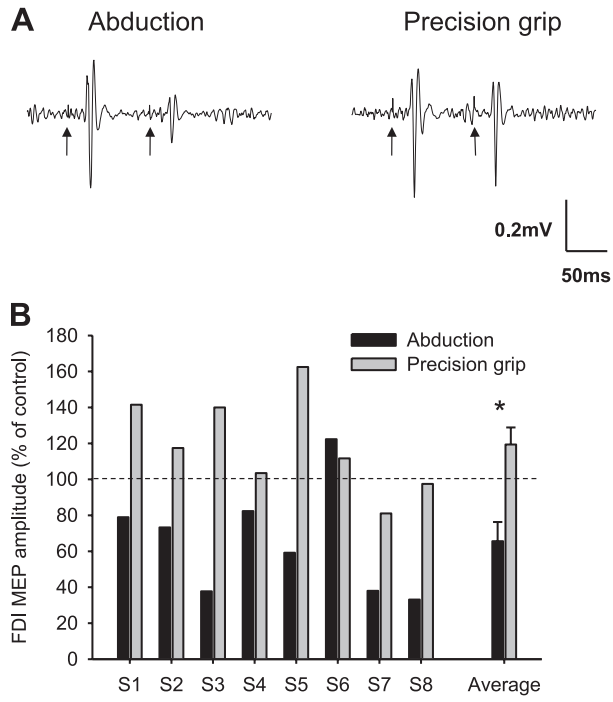

Fig. 6. Long-latency intracortical inhibition in the 2 tasks. *A*: FDI raw recordings. Arrows indicate TMS pulses. The 1st unconditioned MEPs matched in the 2 tasks as well as the EMG background levels. *B*: data obtained in the 8 subjects (S1–S8) and average across subjects (*right*) during abduction (black bars) and precision grip (gray bars). Each bar corresponds to the ratio of conditioned MEP size to unconditioned MEP size represented by the dashed line (100%). *Significant difference ($P < 0.05$).

of cortical excitability resulting from the functional coupling of intracortical circuits controlling the FDI and thenar muscles. The potential mechanisms are discussed below.

Neural mechanisms of I/O curve plateau scaling. We propose that the enhancement of the FDI I/O curves during the precision grip results from decreased inhibition and increased recurrent excitation between the intracortical circuits controlling the FDI and thenar muscles. Simple voluntary contractions, such as index finger abduction, are usually accompanied by a decrease of SICI, which is a reduction of inhibition (Ortu et al. 2008; Ridding et al. 1995). Here, we observed a reduction of SICI during the precision grip task compared with the index abduction task, while ICF remained similar in the two tasks. Thus SICI decreases in going from rest to simple index finger abduction and decreases further during the more complex precision grip task. The present results fully concur with previous observations in a study of the cortical control of the arm during pointing (Devanne et al. 2002). We found that when the ECR muscle was coactive with more proximal arm muscles such as the AD, the plateau of its I/O curve was markedly increased relative to that obtained during its isolated contraction. Accompanying this change, SICI of ECR MEPs was reduced, without changes in ICF (Devanne et al. 2002). Thus task-related coactivation of muscles is accompanied by a reduction of SICI, beyond the reduction that occurs in going from rest to an isolated contraction of an individual muscle.

In the study of Devanne et al. (2002) LICI was not measured. Here, we have shown that LICI was markedly reduced during the precision grip. In five subjects there was, in fact, an apparent facilitation of the test MEP rather than inhibition (Fig. 6*B*), and the ratio of conditioned to unconditioned MEP was close to 100% for two others. Thus, on average, LICI disappeared during precision grip and was even reversed toward facilitation. It was recently shown that TMS-induced LICI is associated with a period of disinhibition that is at first masked by LICI but outlasts LICI and gives rise to a period during which disinhibition predominates and net excitability is increased (Cash et al. 2010). We suggest that this disinhibitory mechanism may be task dependent such that disinhibition occurs earlier during the precision grip. This would lead to a net facilitatory effect when measured at 100 ms, whereas at the same ISI inhibition predominates during index abduction. The functional role of LICI in the operation of the cortical circuitry is, however, unclear (Rosenkranz and Rothwell 2003). What is clear is that we observed a decrease of two measures of intracortical inhibition, SICI and LICI, during the precision grip task. We therefore suggest that such a net disinhibition may, at least in part, underlie the increased plateau of the FDI I/O curve observed in this task. Specifically, we propose the following mechanism for scaling the MEP I/O curve (i.e., changing the plateau) and increasing the recruitment gain without affecting the stimulus threshold. A decrease of intracortical inhibition and an increase of recurrent excitation lead to a larger corticospinal volley at each stimulus intensity. Therefore, a greater proportion of the α-motoneurons in the pool are recruited and at a faster rate, resulting in an increase of the plateau level and recruitment gain. The S_{50} parameter of the I/O curve does not change because the background recruitment level is the same in the two tasks. In this condition, even a minimal descending volley will recruit a proportion of the active motoneurons (Capaday and Stein 1987b). Consequently, the stimulus threshold does not change between tasks. Studies of task-related changes in motor cortical activity, including this one, have consistently found that the plateau value and the recruitment gain of the I/O curves are the two parameters that change significantly and consistently (Capaday et al. 1999; Devanne et al. 2002). Thus measurements of complete I/O curves appear to best reveal changes of cortical excitability (see also Schneider et al. 2002).

Whether the task-dependent changes in intracortical inhibition we observed are of central or peripheral origin cannot be ascertained from the present work. Afferent inputs can affect intracortical inhibitory circuits within the motor cortex (Ridding and Rothwell 1999). For example, topographical reductions of SICI following digit stimulation (Kobayashi et al. 2003; Ridding et al. 2005; Zoghi et al. 2003) or tendon vibration have been demonstrated (Rosenkranz and Rothwell 2003). Thus task-dependent differences in afferent inputs may contribute to changes in intracortical inhibition.

The silent period. It is noteworthy that SP duration was not different in the two tasks investigated. This result is seemingly at odds with a previous study that reported a reduction of SP duration during the precision grip compared with index abduction, suggesting that reduction of SP duration could be one of the possible mechanisms involved in MEP increase during the precision grip (Tinazzi et al. 2003). Details of experimental procedures may explain the differences with our results. First, Tinazzi et al. (2003) used a nonfocal circular coil and measured SP duration at only one stimulus intensity. In our study stimuli were delivered with a focal figure-of-eight coil and we measured complete SP duration I/O curves, which provide more complete and accurate estimates of SP durations (Kimiskidis et al. 2005; Möller et al. 2009). Kimiskidis et al. (2005) compared the classical SP measurement method at one stimulus intensity to measurements of plateau value, S_{50}, and slope of I/O duration curves in epileptic patients. They found that when changes in motor threshold are likely to occur, as in epileptic patients, the I/O method provides results clearly different from the conventional approach (Kimiskidis et al. 2005). Here, the SP I/O curve parameters obtained in the two tasks were statistically indistinguishable, strongly suggesting that the inhibitory processes probed by SP measurements were not involved in the task-related changes of cortical excitability. Given that LICI was task dependent, the common basis of the two inhibitory mechanisms suggested by Werhahn et al. (1999) may be questioned. Indeed, although both SP and LICI are thought to be mediated by $GABA_B$ receptors (McDonnell et al. 2006; Werhahn et al. 1999), several studies suggest that the two processes are associated. Recent findings by McDonnell et al. (2006) indicate that intravenous administration of a single dose of Baclofen increased LICI in healthy subjects but did not modify SP, suggesting that "LICI measures magnitude of inhibition while SP measures duration of inhibition" (McDonnell et al. 2006). Studies on handedness reported higher magnitude of LICI in the cortical hemisphere controlling the preferred hand (Hammond and Garvey 2006), but SP duration was shown to be shorter (Priori et al. 1999). Conversely, during fatiguing exercises, an increase of SP duration has been described (Sacco et al. 1997; Taylor et al. 1996), whereas LICI is reduced (Benwell et al. 2007), suggesting that separate neuronal populations underlie the effect. One population may be upstream of primary motor cortex and related to SP duration,

while a second located within primary motor cortex underlies LICI (Benwell et al. 2007). In any case, here we have shown a complete suppression of LICI during the precision grip, without any change in SP duration. Whatever neural mechanisms underlie the SP duration, they are not involved in the present task-dependent change of MEP I/O curve plateau level we have observed.

Summary and conclusions. Measurements of complete MEP I/O curves obtained during the simple and relatively isolated task of index finger abduction versus those obtained during the precision grip of an object between thumb and index finger clearly revealed a task-dependent change in cortical excitability, manifested by an increase of the I/O curve's plateau level. In conjunction, intracortical inhibition, as measured by SICI and LICI protocols, was reduced during the precision grip task compared with simple index finger abduction. The SP measured from complete I/O duration curves proved not to be task dependent, and the present evidence suggests that SP duration does not fully reflect the strength of inhibition. We proposed that the increase of the I/O curve plateau value during the precision grip was due to a reduction of intracortical inhibition and the associated increase of recurrent excitation between activated cortical loci. Evidence of functional coupling of motor cortical loci by disinhibition and recurrent excitation has been obtained more directly in animal studies (Schneider et al. 2002). Such a coupling may reflect the integrated nature of motor cortical control. That is, task-related muscles, as in the precision grip, are controlled synergistically and not singly and separately (Capaday et al. 2009, 2011; Graziano et al. 2002). This idea, however, does not require that they are controlled via common neural drive.

In closing, we direct the reader's attention to the mirror perspective of the thesis we presented. Intracortical inhibition may be necessary to prevent activation of other muscles when trying to produce pure index abduction, which is a somewhat unnatural task that is easily performed but not commonly done. Thus intracortical inhibition levels may be high under pure abduction conditions but reduced under more natural conditions such as precision grip in order to functionally couple the different cortical muscle representations. This in turn may contribute to the balanced coactivation of the many muscles needed to control force magnitude and direction at the distal tips of the digits. In any case, more investigations are required to understand the neural processes that occur within the motor cortex in the synthesis of motor commands.

ACKNOWLEDGMENTS

We thank Jean-Louis Bourriez for technical assistance and Prof. W. G. Darling for his comments on a draft of the manuscript.

GRANTS

This work was in part supported by a grant from the Nord-Pas de Calais regional council and by a grant to C. Capaday from the Canadian Institutes of Health Research (CIHR).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: N.K.-D., C.C., F.C., and H.D. conception and design of research; N.K.-D., F.C., and H.D. performed experiments; N.K.-D. and H.D. analyzed data; N.K.-D., C.C., F.C., and H.D. interpreted results of experiments; N.K.-D. and H.D. prepared figures; N.K.-D. and H.D. drafted manuscript; N.K.-D., C.C., F.C., P.D., and H.D. edited and revised manuscript; N.K.-D., C.C., F.C., P.D., and H.D. approved final version of manuscript.

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