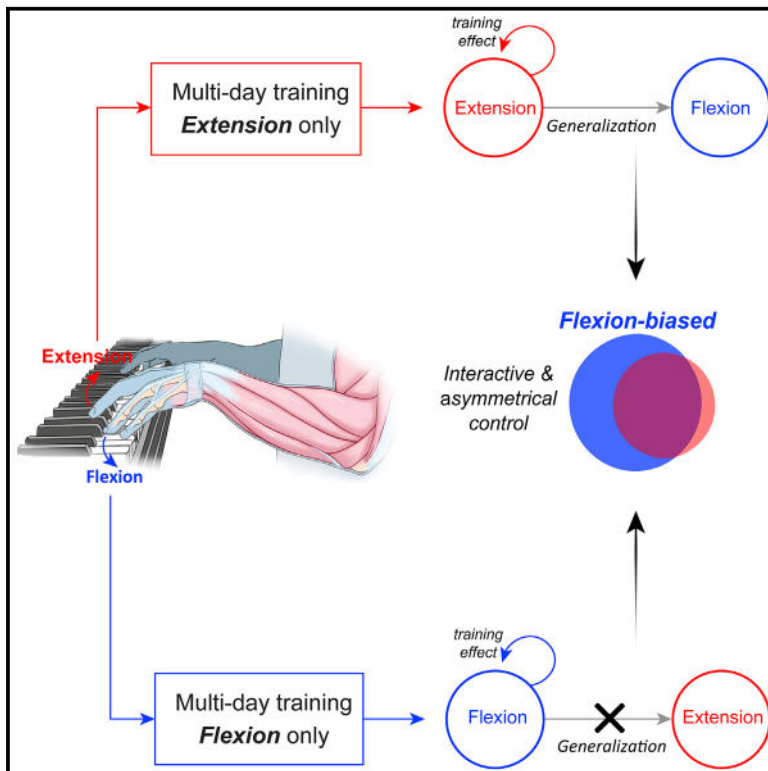


Generalization indicates asymmetric and interactive control networks for multi-finger dexterous movements

Graphical abstract



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In brief

Kamara et al. characterize the behavioral principles underlying the learning and generalization of dexterous flexion and extension movements. They find that the control circuits for learning of finger flexion and extension are interactive in that they partially, but asymmetrically, transfer between directions.

Highlights

- Finger dexterity is manifested by coordination of finger flexion and extension muscles
- Multiday direction-specific training induces inferior dexterity in finger extension
- Learning is dissimilarly transferred between flexion and extension directions
- The data support flexion-biased overlap control of dexterous finger movements



Article

Generalization indicates asymmetric and interactive control networks for multi-finger dexterous movements

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SUMMARY

Finger dexterity is manifested by coordinated patterns of muscle activity and generalization of learning across contexts. Some fingers flex, others extend, and some are immobile. Whether or not the neural control processes of these direction-specific actions are independent remains unclear. We characterized behavioral principles underlying learning and generalization of dexterous flexion and extension movements, within and across hands, using an isometric dexterity task that precisely measured finger individuation, force accuracy, and temporal synchronization. Two cohorts of participants trained for 3 days in either the flexion or extension direction. All dexterity measures in both groups showed post-training improvement, although finger extension exhibited inferior dexterity. Surprisingly, learning of finger extension generalized to the untrained flexion direction, but not vice versa. This flexion bias was also evident in the untrained hand. Our study indicates direction-specific control circuits for learning of finger flexion and extension that interact by partially, but asymmetrically, transferring between directions.

INTRODUCTION

Playing a piano, or simply tying shoelaces, requires precise coordination of multiple fingers, some active in the flexion direction, others in extension and/or other directions and some stay immobile. The ability of the sensorimotor system to control dexterous movements is fundamental to daily life and to survival of higher mammals. This extraordinary dexterous behavior is manifested by generation and use of specific patterns of multi-finger muscle activity when learning complex motor tasks, and further, by generalization of what has been learned in one context to other contexts.^{1,2} Successful coordination of movements with different effectors is particularly evident, for example, when learning to play musical instruments, such as the piano or violin. Individuals initially experience great difficulty in simultaneously producing the appropriate movements across multiple effector muscles and must learn to produce appropriate forces to flex some fingers, while extending or maintaining others immobile, with the proper orientation and configuration varying across different musical notes.

Flexion and extension naturally co-occur in most hand functions and the success in performing these tasks depends on ability to precisely coactivate finger flexor and extensor muscles in both hands. The coexistence of control signals of flexion and extension movements raises the question of whether or not the control processes of these actions are independent or shared. It is presumed that the extent of circuit-sharing between different behaviors depends on the similarities in the patterns of muscle

activation and the state of the limb, such as the effector(s) used or the resultant limb kinematics or dynamics.³ In the case of multi-finger flexor versus extensor movements, the temporal sequence of muscle activations and organization of muscle synergies differ markedly, yet the effector (i.e., fingers) and limb kinematics (e.g., velocity) are quite similar. If the learning circuit encodes only direction-specific muscle patterns, then learning might not be shared or generalized across directions; if it encodes effector or limb kinematics or dynamics, then learning might be shared. To date, the relationship between learning and generalization between flexors and extensors in multi-finger movements in humans is still unknown. We consider two general hypotheses, one of independent control and one of interactive control.

The first possibility is that learning to control finger flexors is independent from, and does not interact with, learning to control extensors (*independent control hypothesis*). Under this hypothesis, learning to produce a particular multi-finger configuration in the flexion direction (e.g., simultaneous flexing of two fingers) should not generalize to the extension direction with the same fingers, and vice versa. In this case, practice would produce learning of novel finger dynamics restricted to the direction within the trained hand. Support for the independent control hypothesis includes a recent high-resolution functional imaging study in humans that reported evidence of two spatially distinct finger maps of finger flexion versus extension in the primary motor cortex (M1).⁴

The second possibility is that learning in the flexion direction is partially shared with learning in the extension direction (*partially*



shared hypothesis), and vice versa. One prediction of this interactive relationship hypothesis is that learning may not be restricted to encoding of specific directions, but rather might involve encoding of the effector(s) being used, regardless of movement direction,⁵ and to some extent, the dynamic involved in the task (e.g., applying 50% of maximum force), that generalizes across directions. In this view, multi-finger flexion-extension coordination would allow rapid and flexible alternation of finger movements in fine-motor control during dexterous movements. Support for the shared information between different muscle groups is the finding that in primates, single neurons in M1 receive common sensory input about the shoulder and elbow joints, but the output is largely specific to movements about the shoulder, potentially to allow rapid corrective responses to mechanical arm perturbation.⁶ Within this general hypothesis there are two options; generalization is either symmetrical or asymmetrical. While it may be intuitive to hypothesize symmetric generalization from flexion to extension, and vice versa, this is not necessarily true. First, pre-existing bias of flexion is evident by the ability to more precisely control movements of finger flexors compared with extensors.⁷ Second, stroke survivors with cortical lesion, who, despite regaining good flexion-based grasp, have very weak finger and wrist extensors that heavily prevent hand opening.^{8–13} Third, a recent neurophysiological study showed increased representation of finger flexors, but weaker representation of finger extensors, following micro-stimulation of the human motor cortex.¹⁴

Thus, here we sought evidence supporting one of the two general hypotheses, or a variation of them, in an effort to advance the understanding of neural control of hand dexterity. As such, we aimed to characterize the behavioral principles underlying the control process, learning ability, and generalization of single and multi-finger dexterous movements in the flexion and extension directions, through a finger dexterity task. We decomposed dexterity into its underlying components: *finger individuation*, defined as the ability to independently move instructed finger(s), either in a flexion or extension direction, while keeping uninstructed fingers immobile (minimizing enslaving); *force control*, defined as the ability to generate accurate force of the instructed finger(s); and *temporal synchronization*, defined as the ability to produce simultaneous movement between instructed finger(s).

Following 3-day training in two separate groups on a multi-finger dexterity task in either the flexion or extension direction, we observed improvement in all dexterity measures in both groups, although inferior dexterity in the extension direction. Interestingly, we observed asymmetric generalization across directions. That is, learning generalized from the extension to flexion direction, but not vice versa, in the trained hand. Based on the results of the current study, we propose a refined version of the partially shared hypothesis for dexterity control, the *biased-overlap hypothesis*, which predicts partially shared control, but different generalization patterns across directions and hands that depend on the trained direction. Our findings corroborate this hypothesis that controlling multi-finger dexterous patterns is direction-specific, and that learning is dissimilarly transferred between directions, suggesting that neural control circuits for learning of finger flexion and extension interact and partially, but asymmetrically, overlap in the sensorimotor system.

RESULTS

The primary aim of this study was to characterize learning and generalization of finger dexterity in the flexion and extension directions. Two cohorts of healthy young participants (flexor and extensor groups) were trained with the dominant right hand over three sessions (days 2–4), on an isometric single and multi-finger chord-like task in the flexion or extension direction, respectively. Pre- and post-training testing was conducted on days 1 and 5 (Figure 1C). We quantified the learning effect within the trained direction using multiple dexterity measures, and then generalization of learning to the untrained direction (directional generalization) and untrained hand (lateral generalization). A control group underwent testing on days 1 and 5, but not training.

During the study, participants placed both hands in a neutral posture in an adjustable ergonomic device with force sensors positioned below and above each fingertip to measure isometric flexion and extension forces, respectively (Figure 1A). Prior to testing on day 1, maximum voluntary force (MVF) of each finger was measured using the “MVF Task” to set target levels for testing and training (Figure 1B, left). During testing and training (days 1–5), participants were instructed to move only the relevant fingers to the appropriate target forces while maintaining uninstructed fingers at rest. Initial baseline (day 1) and post-training (day 5) measurements were obtained using the “Single-Finger Task” and “Multi-Finger Task” (Figure 1B, middle and right, respectively) in both flexion and extension directions. Training (days 2–4) was performed using the same single and multi-finger tasks, but only in the direction in accordance with group type.

Within-direction learning of flexion and extension multi-finger actions

During training (days 2–4), participants performed 31 finger combinations, in pseudo-random order, a total of 10 times during 5 blocks (2 repetitions of each combination in each block). Each group trained only in their respective direction.

Dexterity was characterized by three main quantifiable components: *finger individuation*, defined as ability to independently move instructed finger(s), either in the flexion or extension direction, while keeping uninstructed fingers immobile (minimizing enslaving) (Figures 2A, 2B, and 2D); *force control*, defined as ability to generate accurate force of instructed finger(s) (Figures 2C and 2E); and *temporal synchronization*, defined as ability to produce accurate timing between instructed fingers (Figures 2A and 2F). The values in the following subsections represent within-direction learning metrics during the training period.

Accuracy as a measure of force control

The accuracy of each trial was described by *meanDevI* (see STAR Methods). Lower *meanDevI* indicates more accurate achievement of target forces with instructed finger(s). Improvement in accuracy during the training period can be seen by the decreasing trend in Figure 3A. Deviation values were normalized by MVF to enable comparison between the two groups and their respective directions. The daily averages (\pm SE) of the flexor group were 8.73% (\pm 0.14%) (day 2), 7.75% (\pm 0.07%) (day 3), 6.90% (\pm 0.06%) (day 4), with an improvement of (9.50% – 6.82%) = 2.68% between the first and last blocks. The daily averages of the extensor group were 11.27% (\pm 0.17%), 9.94%

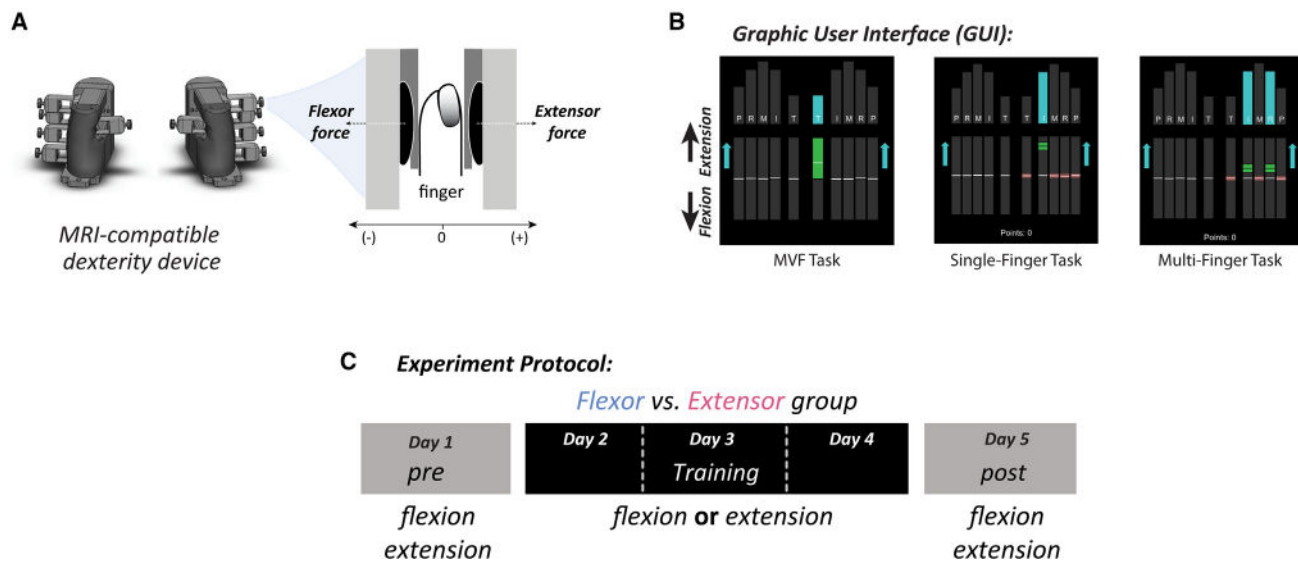


Figure 1. Experimental setup, protocol, and hypothesis

(A and B) (A) Ergonomic device used to measure isometric finger flexion and extension forces via force sensors, as seen in top view on the right. (B) Graphic user interface (GUI). Left diagram shows the GUI during the MVF task, specifically during the MVF measurement of right thumb extension. Middle diagram shows the GUI during an individuation (single-finger) task in which participants were asked to extend their right index to 75% MVF. Diagram on right shows the GUI during a chord (multi-finger) task in which participants were asked to extend their right index and ring finger simultaneously to 25% MVF. (C) Experimental protocol was partitioned into three sections: pre-training testing, training, and post-training testing. All four movement types (RH and LH, both flexion and extension) were done on testing days, although only RH flexion or extension was done during training, according to group type.

($\pm 0.13\%$), 9.40% ($\pm 0.10\%$), with an improvement of (12.16% – 9.46%) = 2.70% between the first and last blocks. The flexor group was consistently more accurate than the extensor group, although both groups had similar trends of improvement. This can be seen by the two-way (time vs. group) RM-ANOVA, which showed a significant time effect as a result of the training ($F(1,23) = 87.28$, $p < 0.0001$), as well as a significant difference between the two groups ($F(1,23) = 22.65$, $p < 0.0001$), although there was no significant interaction between the time and group factors ($F(1,23) = 2.865$, $p = 0.104$).

Uninstructed finger deviation (enslaving)

The uninstructed finger deviation of each trial was described by *meanDevU* (see STAR Methods). Lower *meanDevU* indicates less enslaving of uninstructed fingers. Improvement in minimizing enslaving can be seen by the trend of decreasing deviation during the training period (Figure 3B). Values were also normalized by MVF here. The daily averages (\pm SE) of the flexor group were 4.43% ($\pm 0.11\%$), 3.83% ($\pm 0.15\%$), 3.39% ($\pm 0.06\%$), with an improvement of (4.82% – 3.31%) = 1.52% between the first and last blocks. The daily averages of the extensor group were 4.56% ($\pm 0.11\%$), 4.13% ($\pm 0.14\%$), 4.03% ($\pm 0.06\%$), with an improvement of (5.23% – 4.18%) = 1.05% between the first and last blocks. Two-way (time vs. group) RM-ANOVA showed a significant time effect as a result of the training ($F(1,22) = 40.28$, $p < 0.0001$), although there was no significant difference between the two groups ($F(1,23) = 0.1639$, $p = 0.8993$) nor any significant interaction between the time and group factors ($F(1,22) = 1.073$, $p = 0.3115$). Although the flexor and extensor groups had similar initial values, the flexor group had greater improvement during the training.

Reaction time

During multi-finger targets, the reaction time (RT) was selected as the minimal timestamp of the various instructed fingers. Due to the randomized order of finger combinations, participants could not anticipate and/or plan their motion prior to the visual cues. The daily averages (\pm SE) of the flexor group were 707.9 (± 18.3) ms, 590.4 (± 11.6) ms, 555.5 (± 9.0) ms, with an improvement of (791.9 – 546.8 ms) = 245.1 ms between the first and last blocks. The daily averages of the extensor group were 790.4 (± 22.8) ms, 692.9 (± 12.2) ms, 643.7 (± 10.8) ms, with an improvement of (924.9 – 642.5) = 282.4 ms between the first and last blocks. Two-way (time vs. group) RM-ANOVA showed a significant time effect as a result of the training ($F(1,22) = 27.09$, $p < 0.0001$), although there was no significant difference between the two groups ($F(1,22) = 0.618$, $p = 0.4401$) nor any significant interaction between the time and group factors ($F(1,22) = 0.861$, $p = 0.3635$), suggesting that both groups similarly improved their RT.

Temporal synchronization during multi-finger actions

Degree of synchronization among multi-finger actions was described by the standard deviation between the various instructed finger reaction times. Lower standard deviation indicates more synchronous motion. The daily averages (\pm SE) of the flexor group were 355.5 (± 5.0) ms, 306.0 (± 5.7) ms, 286.2 (± 0.3) ms, with an improvement of (367.4 – 258.7 ms) = 108.7 ms between the first and last blocks. The daily averages of the extensor group were 609.9 (± 3.0) ms, 542.0 (± 13.4) ms, 511.9 (± 8.7) ms, with an improvement of (598.3 – 405.7) = 192.6 ms between the first and last blocks. Here, the flexor group had significantly better temporal synchronization than the

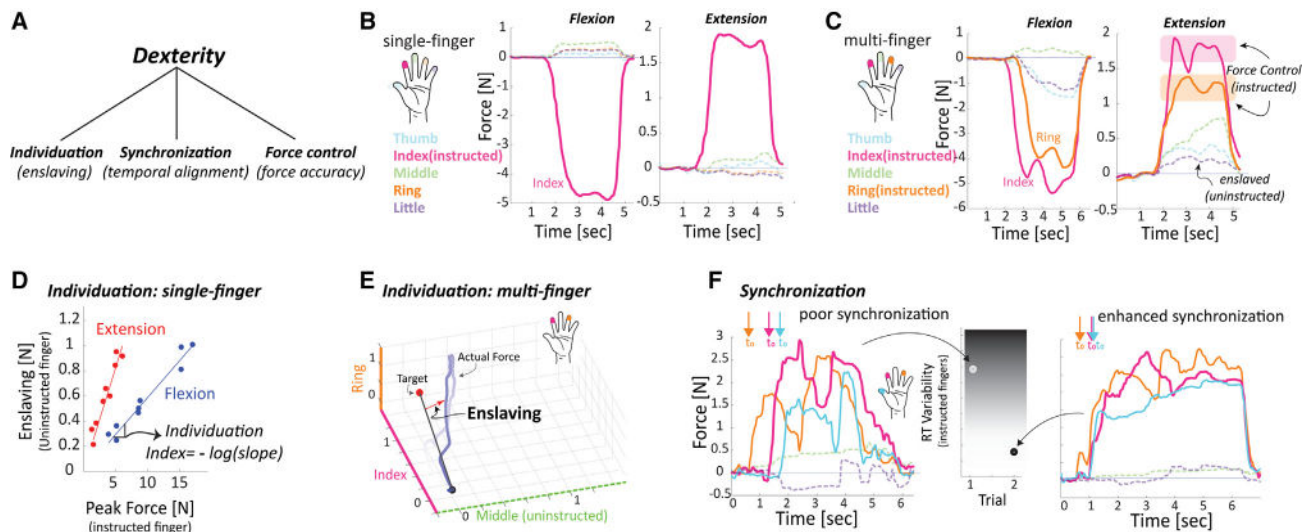


Figure 2. Visual descriptions of measurable metrics

(A) Dexterity is characterized by three main quantifiable components.

(B) Example of single-finger flexion and extension trials, specifically isolated finger movements. Flexion forces were assigned negative values and extension forces had positive values. Force targets were set according to each finger's MVF.

(C) Examples of multi-finger flexion and extension trials, specifically index and ring finger movements. MeanDevI was calculated for the instructed fingers' force profiles around the target forces, as seen in highlighted regions. MeanDevU was calculated over the same timeframe from the uninstructed fingers' forces, produced due to enslaving.

(D) Individuation Index of each finger was calculated as $-\log$ of the slope between peak active force and uninstructed finger deviation. This graph contains the nine extension (red) and nine flexion (blue) trials (three repetitions of three force levels) of a single finger.

(E) A 3D representation of the enslaving which occurs during multi-finger movements.

(F) Poor temporal synchronization can be seen in left trial of multi-finger trials compared with a trial with enhanced temporal synchronization. Movement onset of different instructed fingers noted with arrows.

extensor group, although both showed improvement during training. Two-way (time vs. group) RM-ANOVA showed a significant time effect as a result of the training ($F(1,22) = 23.23$, $p < 0.0001$), as well as a significant difference between the two groups ($F(1,22) = 20.78$, $p = 0.0002$), although there was no significant interaction between the time and group factors ($F(1,22) = 0.2624$, $p = 0.6136$). Figure 3C shows the improvement in synchronization over the course of training for both groups.

Individuation index

Individuation indices (IIs) were measured on the first and last day and reported here for the right hand only. Higher II indicates better individuation (see Table S2 for full results). On the first day, the overall hand flexion II (\pm SE) average of the flexor group was 2.36 (± 0.16). Following training, the overall hand flexion II (\pm SE) average of the flexor group was 2.65 (± 0.17), resulting in an improvement of $\Delta = 0.29$ (Figure 4A, top panel). Post hoc two-tailed, paired sample t test comparison between performance on day 5 and day 1 showed that training led to significant improvement in flexion II values ($t(12) = 3.717$, $p = 0.003$). Similarly, the extensor group also showed positive change in overall II following training (Figure 4A, bottom panel). Overall hand extension II (\pm SE) pre-training was 2.25 (± 0.17). Following training, overall hand extension II (\pm SE) was 2.58 (± 0.14), resulting in an improvement of $\Delta = 0.33$. Post hoc paired two-tailed, sample t test comparison between performance on day 5 and day 1 showed that training led to significant improvement in extension II values ($t(12) = 3.006$, $p = 0.011$). These results

show that both groups similarly improved overall II in their trained direction.

Directional generalization

Movements in the opposite direction of the training were performed and assessed only on the first and last day and reported here for the right hand only. The extension II (\pm SE) of the flexor group was 2.16 (± 0.14) prior to training, and 2.31 (± 0.13) following training, resulting in an improvement of $\Delta = 0.15$ (Figure 4A, top panel). Two-way (time vs. direction) RM-ANOVA for the flexor group showed a significant effect for both time ($F(1,12) = 6.40$, $p = 0.0264$) and direction parameters ($F(1,12) = 7.39$, $p = 0.0187$), and time \times direction interaction effect of $p = 0.0569$ ($F(1,12) = 4.43$). While the flexor group improved II in the trained flexion direction, post hoc two-tailed, paired sample t test comparison between performance on day 5 and day 1 showed that training did not lead to significant improvement in extension II values ($t(12) = 1.085$, $p = 0.299$). Asymmetry between flexion and extension IIs in the trained hand can be seen in Figure 4D, which shows a rather consistent improvement among all fingers in the flexion motion, although only a slight difference in individual finger II values for extension. For the extensor group, the flexion II (\pm SE) was 2.01 (± 0.18) pre-training, and 2.62 (± 0.17) post-training, with an improvement of $\Delta = 0.61$ (Figure 4A, bottom panel). Two-way (time vs. direction) RM-ANOVA for the extensor group showed a significant effect for the time parameter ($F(1,12) = 23.97$, $p = 0.0004$), although not for the direction

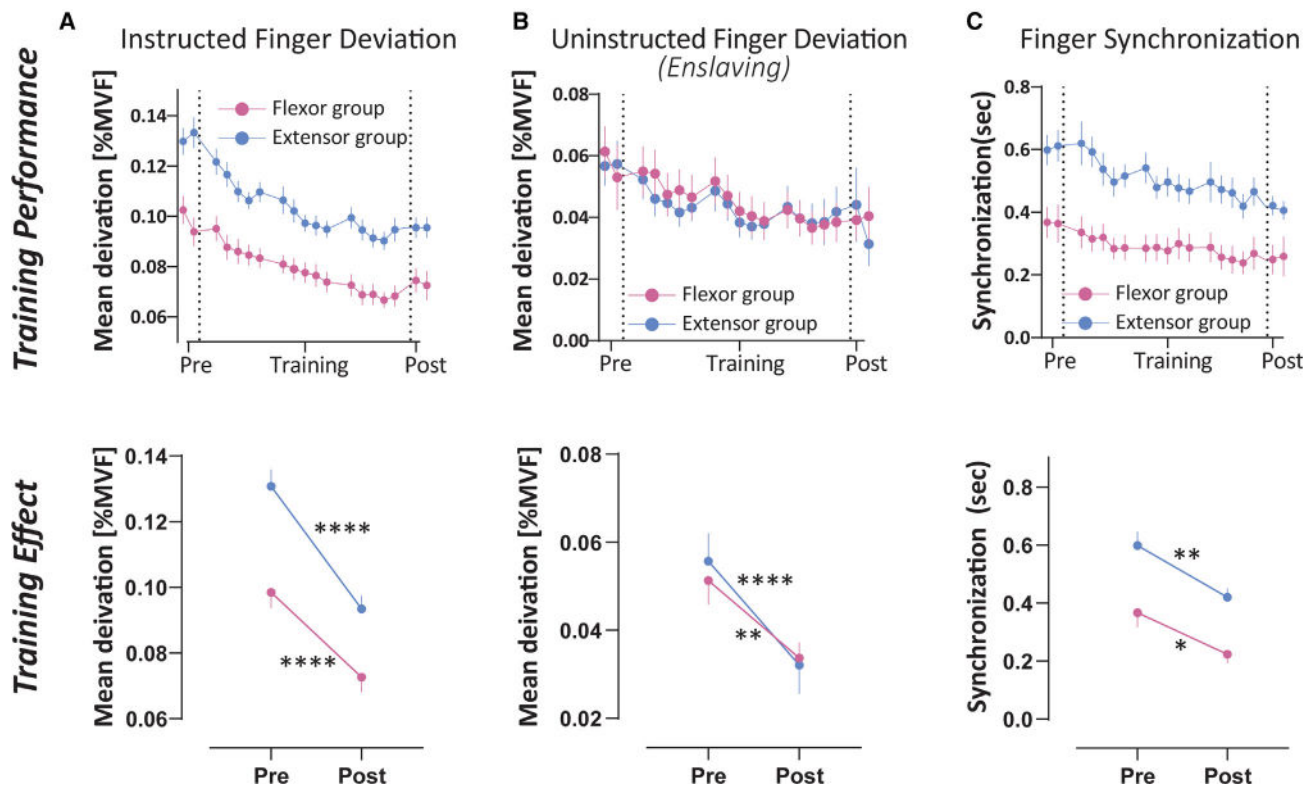


Figure 3. Performance during training period and training effect in the various metrics on the trained hand and trained direction of both flexor and extensor groups

Training performance metrics represent average performance in each of the 19 blocks; pre- and post- values are the average performance during the averaged values of the two testing blocks.

(A) Force control metric is depicted using “instructed finger deviation,” or MeanDevI, normalized by MVF.

(B) Uninstructed finger deviation, or MeanDevU, normalized by MVF.

(C) Temporal synchronization between fingers.

Bars represent mean and error bars represent s.e. of the mean. * for $p < 0.05$, ** for $p < 0.01$, and **** for $p < 0.0001$.

parameter ($F(1,12) = 0.3926$, $p = 0.5427$), and time \times direction interaction effect of $p = 0.0657$ ($F(1,12) = 4.10$). Interestingly, post hoc two-tailed, paired sample t test comparison between performance on day 5 and day 1 showed that training led to significant improvement in flexion II values in the extensor group ($t(12) = 6.127$, $p < 0.0001$). Increased flexion and extension IIs in the extensor group can be seen in Figure 4E, which shows improvement among all fingers in both directions. A comparison between Figures 4D and 4E further reveals the effect of the trained direction on the learning and generalization abilities. These results depict asymmetry in directional generalization.

To rule out any confounds arising from differences in baseline II values between the flexion-trained and extension-trained groups in our data, we performed an analysis of covariance (ANCOVA). ANCOVA on the extension direction (comparing post-training to pre-training while controlling for the pre-training value as a covariate) revealed significant difference ($F = 4.38$, $p = 0.04$) in the extension direction between groups. Combining this result and the significant change only in the extensor group in the extension direction, clearly indicates that only the extension-trained group improved, regardless of possible differences at baseline. In the flexion direction, the ANCOVA test (comparing

post-training to pre-training while controlling for the pre-training value as a covariate) did not reveal significant difference ($F = 0.02$, $p = 0.87$) between groups, despite the difference at baseline, indicating similar post-training improvement. Combining this result and the significant change in both groups in the flexion direction, suggests that both groups changed their flexion II and reached similar levels, regardless of differences in baseline flexion direction.

Temporal synchronization of extension in the flexor group was $618.7 (\pm 79.2)$ ms before training and $568.8 (\pm 68.4)$ ms following training, resulting in an improvement of $\Delta = 49.9$ ms (Figure 4B, top panel). Two-way (time vs. direction) RM-ANOVA for the flexor group showed a significant effect for the direction parameter ($F(1,11) = 19.10$, $p = 0.0011$), but not for the time parameter ($F(1,11) = 3.793$, $p = 0.0774$). There was a time \times direction effect ($F(1,11) = 7.043$, $p = 0.0224$). For the extensor group, flexion synchronization (\pm SE) was $519.0 (\pm 52.9)$ ms before training and $412.3 (\pm 42.1)$ ms following training, resulting in an improvement of $\Delta = 106.7$ ms (Figure 4B, bottom panel). Two-way (time vs. direction) RM-ANOVA for the extensor group showed a significant effect for both the time parameter ($F(1,11) = 20.44$, $p = 0.0009$) and the direction parameter ($F(1,11) = 14.15$, $p = 0.0031$),

Trained Hand Performance

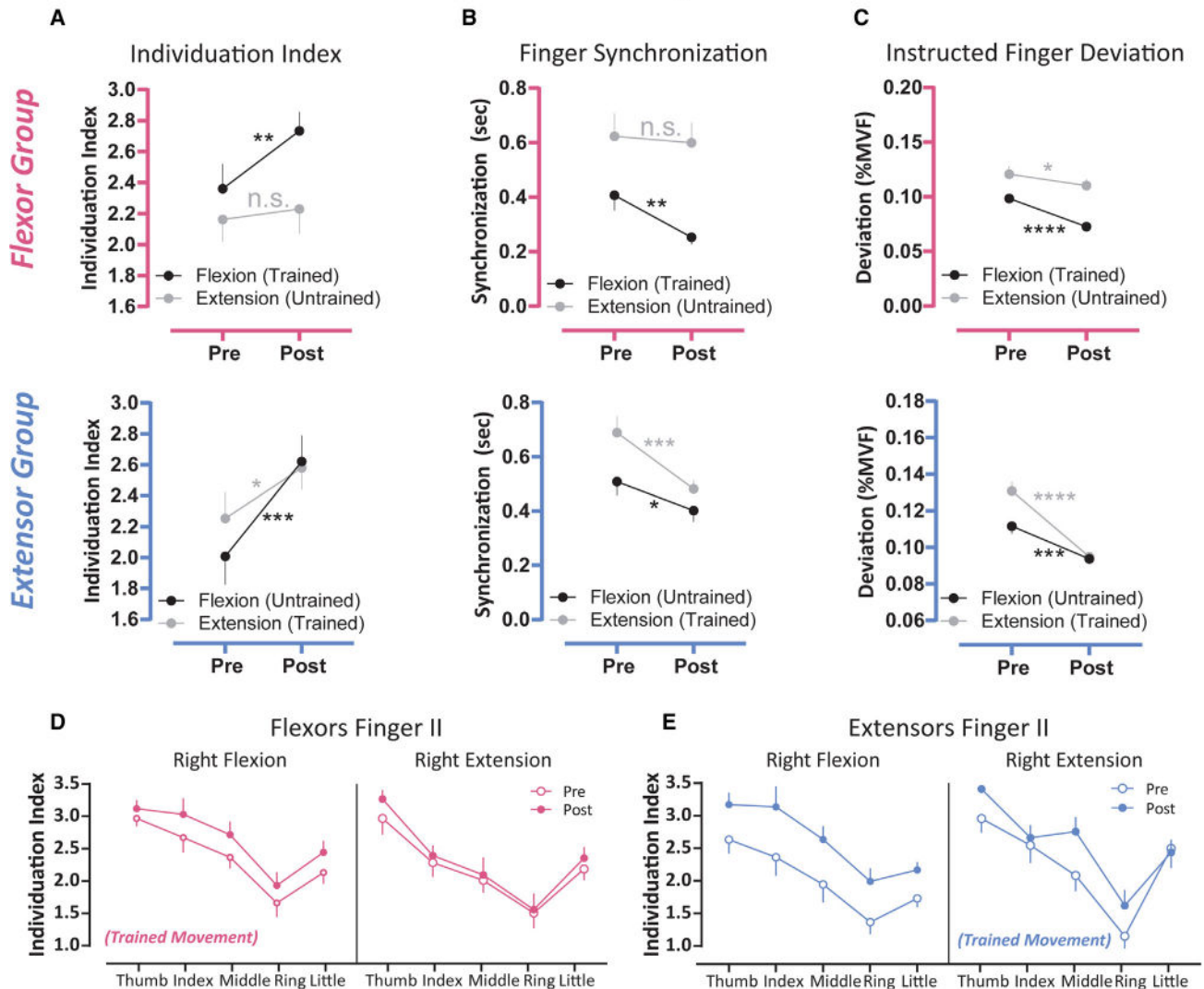


Figure 4. Asymmetric generalization of finger dexterity measures across directions of the trained hand of both flexor and extensor groups

(A) Training effect on values of Individuation Index.

(B) Same as (A) but for changes in temporal synchronization between fingers.

(C) Same as (A) but for force control, as calculated by MeanDevi, normalized by MVF.

(D) Flexor group's finger II values on RH flexion and RH extension, pre- and post-training.

(E) Extensor group's finger II values on RH flexion and RH extension, pre- and post-training.

Bars represent mean and error bars represent s.e. of the mean. * for $p < 0.05$, ** for $p < 0.01$, *** for $p < 0.001$, **** for $p < 0.0001$, and n.s. for not significant.

although there was no interaction between the two ($F(1,11) = 3.315$, $p = 0.0960$).

Accuracy of extension in the flexor group was $0.120 (\pm 0.0068)$ before training and $0.110 (\pm 0.006)$ following training, resulting in an improvement of $\Delta = 0.01$ (Figure 4C, top panel). Two-way (time vs. direction) RM-ANOVA for the flexor group showed a significant effect for both the time parameter ($F(1,11) = 16.97$, $p = 0.0017$) and direction parameter ($F(1,11) = 32.23$, $p = 0.0001$), as well as an interaction between the two ($F(1,11) = 9.840$, $p = 0.0095$). For the extensor group, flexion accuracy (\pm SE) was $0.1123 (\pm 0.0051)$ before training

and decreased to $0.1109 (\pm 0.0346)$ after training, resulting in an improvement of $\Delta = 0.0054$ (Figure 4C, bottom panel). Two-way (time vs. direction) RM-ANOVA for the extensor group showed a significant effect for both the time ($F(1,11) = 62.32$, $p < 0.0001$) and direction parameter ($F(1,11) = 10.62$, $p = 0.0068$), as well as an interaction between the two ($F(1,11) = 11.49$, $p = 0.0069$).

Across hands generalization

Movements of the opposite hand (left hand; LH) were only performed and assessed on the first and last day. LH flexion II

Untrained Hand Performance

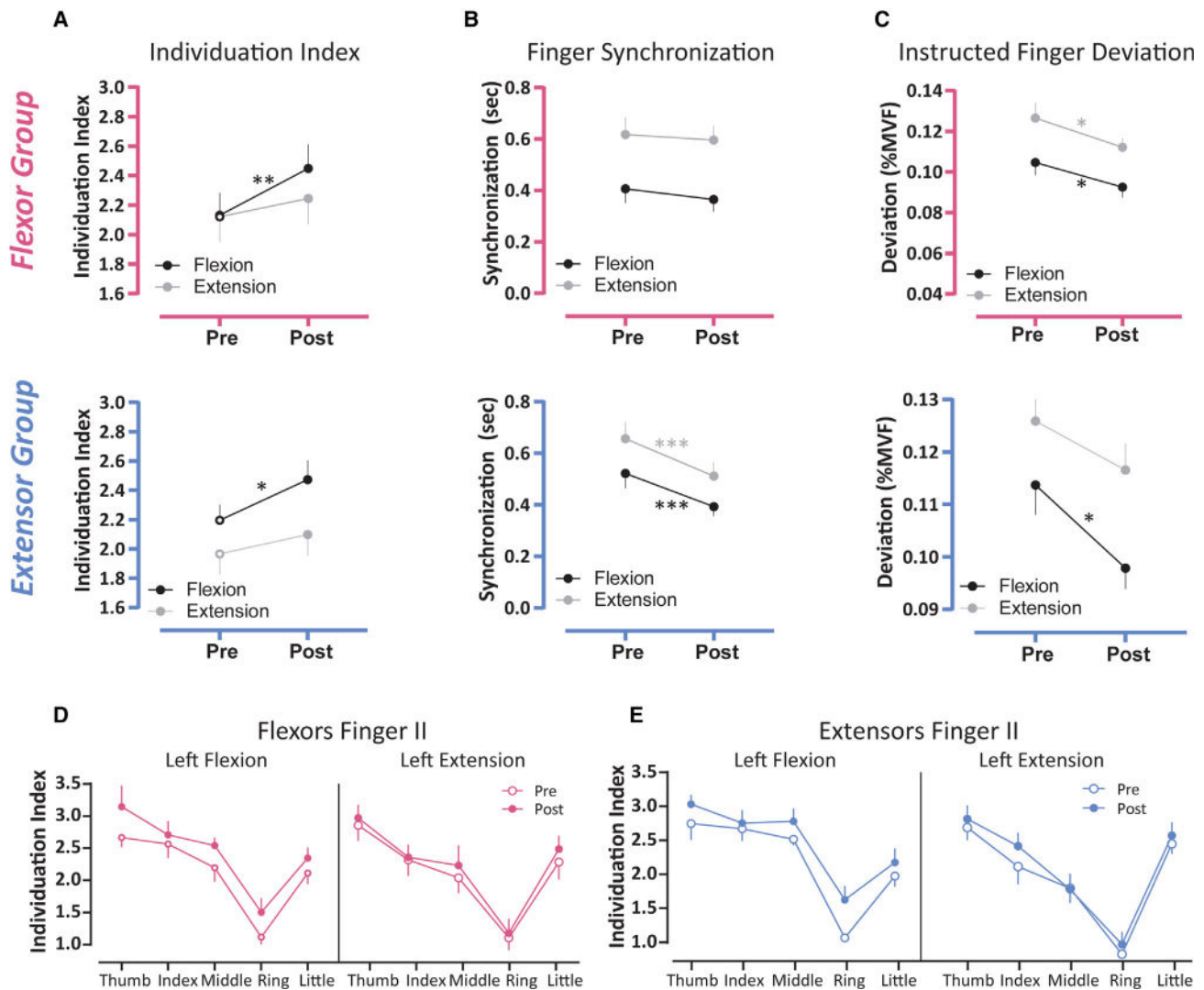


Figure 5. Generalization of finger dexterity measures across hand, on left hand (untrained) movements for both flexor and extensor groups
 (A) Training effect changes in Individuation Index.
 (B) Same as (A) but for changes in temporal synchronization between fingers.
 (C) Same as (A) but for force control, as calculated by MeanDevl, normalized by the MVF.
 (D) Flexor group's finger II values on LH flexion and LH extension, pre- and post-training.
 (E) Extensor group's finger II values on LH flexion and LH extension, pre- and post-training.
 Bars represent mean and error bars represent s.e. of the mean. * for $p < 0.05$, ** for $p < 0.01$, *** for $p < 0.001$, **** for $p < 0.0001$, and n.s. for not significant.

(\pm SE) was 2.13 (\pm 0.15) before training and 2.45 (\pm 0.16) following training, resulting in an improvement of $\Delta = 0.32$ (Figure 5A, top panel). Two-way (time vs. direction) RM-ANOVA for the flexor group showed a significant effect for the time parameter ($F(1,12) = 7.30, p = 0.0192$), although not for the direction parameter ($F(1,12) = 0.61, p = 0.4474$), nor an interaction between the two ($F(1,12) = 3.09, p = 0.1042$). Post hoc two-tailed, paired sample t test comparison between performance on day 5 and day 1 showed that training led to significant improvement in LH flexion II values ($t(12) = 4.103, p = 0.003$). For the extensor group, the LH

extension II (\pm SE) average was 1.97 (\pm 0.14) before training and increased to 2.10 (\pm 0.14) after training, resulting in an improvement of $\Delta = 0.13$ (Figure 5A, bottom panel). Two-way (time vs. direction) RM-ANOVA for the extensor group showed a significant effect for both time ($F(1,12) = 4.85, p = 0.0478$) and direction parameters ($F(1,12) = 6.85, p = 0.0224$), although no interaction between the two ($F(1,12) = 1.45, p = 0.2503$). Post hoc two-tailed, paired sample t test comparison between performance on day 5 and day 1 showed that training did not lead to significant improvement in LH extension II values ($t(12) = 1.556, p = 0.146$).

This, again, reveals asymmetry in generalization patterns depending on the trained motion.

Temporal synchronization of LH flexion of the flexor group was 399.6 (\pm 54.4) ms before training and 374.5 (\pm 48.3) ms following training, resulting in an improvement of $\Delta = 25.1$ ms (Figure 5B, top panel). Two-way (time vs. direction) RM-ANOVA for the flexor group showed a significant effect for the direction parameter ($F(1,11) = 25.85$, $p = 0.0004$), although not for the time parameter ($F(1,11) = 0.519$, $p = 0.4863$), nor an interaction between the two ($F(1,11) = 0.1413$, $p = 0.7141$). For the extensor group, LH extension synchronization (\pm SE) was 663.3 (\pm 64.2) ms before training and decreased to 518.0 (\pm 54.9) ms following training, resulting in an improvement of $\Delta = 145.2$ ms (Figure 5B, bottom panel). Two-way (time vs. direction) RM-ANOVA for the extensor group showed a significant effect for both the time ($F(1,11) = 7.03$, $p = 0.0225$) and direction parameter ($F(1,11) = 22.91$, $p = 0.0006$), although no interaction between the two ($F(1,11) = 0.1578$, $p = 0.6988$).

Accuracy of LH flexion in the flexor group was 0.102 (\pm 0.0056) before training and 0.0925 (\pm 0.005) following training, resulting in an improvement of $\Delta = 0.0095$ (Figure 5C, top panel). Two-way (time vs. direction) RM-ANOVA for the flexor group showed a significant effect for both the time ($F(1,11) = 11.28$, $p = 0.0064$) and direction parameter ($F(1,11) = 57.54$, $p < 0.0001$), although no interaction between the two ($F(1,11) = 0.1439$, $p = 0.7117$). For the extensor group, LH extension accuracy (\pm SE) was 0.1275 (\pm 0.0053) before training and decreased to 0.1329 (\pm 0.0228) following training, resulting in an improvement of $\Delta = 0.0054$ (Figure 5C, bottom panel). Two-way (time vs. direction) RM-ANOVA for the extensor group showed a significant effect for both the time ($F(1,11) = 5.507$, $p = 0.0369$) and direction parameter ($F(1,11) = 21.25$, $p = 0.0006$), as well as an interaction between the two ($F(1,11) = 10.67$, $p = 0.0085$).

We also investigated the combination of both lateral and directional generalization, i.e., movement in the opposite hand and opposite direction of the trained movement. For the flexor group, LH extension II (\pm SE) was 2.12 (\pm 0.17) before training and 2.25 (\pm 0.18) after training, resulting in an improvement of $\Delta = 0.13$ (Figure 5A, top panel). Post hoc two-tailed, paired sample *t* test comparison between performance on day 5 and day 1 showed that training did not lead to significant improvement in LH extension II ($t(12) = 1.617$, $p = 0.132$). The extensor group, however, did have significant improvement in LH flexion II. The extensor group's average LH flexion II was 2.20 (\pm 0.11) before training and 2.47 (\pm 0.13) after training, resulting in an improvement of $\Delta = 0.27$ (Figure 5A, bottom panel). Post hoc two-tailed, paired sample *t* test comparison between performance on day 5 and day 1 showed that training led to significant improvement in LH flexion II values ($t(12) = 3.264$, $p = 0.014$). Figures 5D–5F shows the individual fingers' II values in both directions, and clearly shows the lack of improvement in LH extension in both groups, although a slight improvement across all fingers in LH flexion for both the flexor and extensor groups.

Control experiment

To rule out the possibility that the observed improvement in dexterity was due to re-exposure to the test itself and not generalization of what was learned, a control group was tested on day 1

and day 5 only (Figure S4). None of the dexterity measures showed significant improvement between day 1 and day 5. For example, right hand (RH) II revealed a non-significant time effect ($p = 0.850$) and no time \times direction interaction effect ($p = 0.200$). Specifically, RH flexion II was 2.57 (\pm 0.11) on day 1 and 2.64 (\pm 0.09) on day 5, resulting in a change of 0.12. RH extension II was 2.43 (\pm 0.14) on day 1 and 2.31 (\pm 0.14) on day 5, resulting in a decrease of 0.12. LH flexion II was 2.79 (\pm 0.13) on day 1 and 2.73 (\pm 0.10) on day 5, resulting in a decrease of 0.06. LH extension II was 2.59 (\pm 0.12) on day 1 and 2.61 (\pm 0.09) on day 5, resulting in a change of only 0.02. LH II also showed a non-significant time effect ($p = 0.851$) and no time \times direction interaction effect ($p = 0.334$). Changes in finger synchronization were as follows: RH flexion $\Delta = -36$ ms, RH extension $\Delta = -54$ ms, LH flexion $\Delta = -48$ ms, and LH extension $\Delta = 65$ ms. Changes in instructed finger deviation were as follows: RH flexion $\Delta = -1.1\%$ MVF, RH extension $\Delta = -0.4\%$ MVF, LH flexion $\Delta = -0.8\%$ MVF, and LH extension $\Delta = 0.5\%$ MVF. Changes in uninstructed finger deviation were as follows: RH flexion $\Delta = -0.4\%$ MVF, RH extension $\Delta = -0.7\%$ MVF, LH flexion $\Delta = 0.0\%$ MVF, and LH extension $\Delta = -0.1\%$ MVF. The lack of significant change in performance supports that the training is the main cause for the improvement seen in the flexor and extensor groups. Moreover, these data strongly suggest that the asymmetric, direction-dependent effects we observed in the main experiment are attributed to the generalization of learning and not to re-exposure to the test, nor to passage of time.

Difficulty effect in generalization

Next, we tested if the improvement in dexterity was due to difference in difficulty between flexion and extension tasks. We first defined a 2-dimensional difficulty space based on mean deviation of the instructed fingers and execution time of all single and multi-finger movements in the flexion and extension direction. Based on the distance of the averaged performance across all participants for each chord from the origin of this difficulty space, we categorized performance in flexion and extension into three levels: low, medium, and high difficulty (Figures 6A and 6B). Our data ruled out that asymmetric biases between flexion and extension were simply because extension tasks were more difficult than flexion. We found no significant effect of difficulty in decreased uninstructed finger deviation ($p = 0.373$) nor significant difficulty \times group interaction effect in the extension direction ($p = 0.489$). Similar results were observed in the flexion direction with no significant effect of difficulty in decreased uninstructed finger deviation ($p = 0.988$) nor significant difficulty \times group interaction effect ($p = 0.317$) (Figure 6C). The lack of significant correlation between task difficulty and generalization of finger dexterity supports our main conclusion of asymmetric and interactive control for multi-finger flexion and extension dexterous movements.

DISCUSSION

Our study provides detailed characterization of dexterous single and multi-finger flexion and extension movements in humans. Dexterity components (finger individuation, force control, and

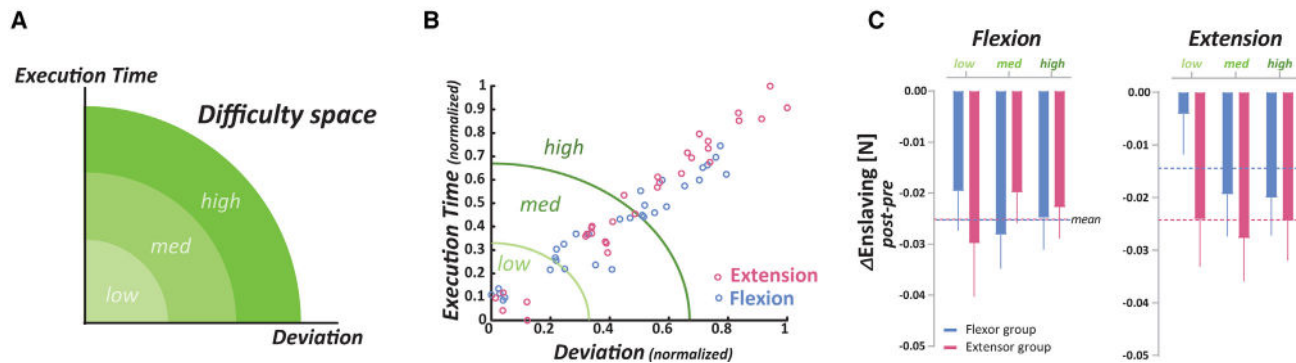


Figure 6. No effect of difficulty on generalization

(A) Difficulty space was defined based on execution time and deviation of instructed fingers (i.e., inverse to accuracy) in day 1.

(B) Characterizing chords of flexion and extension in the difficulty space to low, medium, and high. Each marker represents averaged performance of a specific chord across all participants.

(C) Change in enslaving (*post-pre*) in both groups and each direction. We found no significant difficulty effect nor difficulty \times group effect on generalization.

temporal synchronization) were investigated individually and collectively to shed light on motor learning abilities during a training period, as well as changes after the training period. Our goal was to further define the control mechanisms affecting multi-finger dexterous movement, specifically learning and generalization of flexion and extension.

Training effect on multi-finger dexterity components

In order to illuminate potential relationships of the neural control mechanisms, two healthy cohorts were randomly assigned to train on either flexion or extension movements. Differing values between the groups can be seen within the first blocks of training, especially in accuracy and synchronization (Figure 3). Baseline values revealed enhanced accuracy and synchronization in the flexion direction compared with extension, likely due, in part, to extension motions being less common in daily functions, and therefore less skilled. Also, Yu et al.¹⁵ revealed higher force deficit (less accuracy) in extension movements compared with flexion in production of maximal contractions. Support for the flexor-biased observation comes from reports of focal hand dystonia in pianists that typically occurs in the direction of finger flexion, but not extension,^{16,17} although healthy pianists use a combination of finger flexion and extension in preparation for subsequent successful keypresses.^{18,19} Altogether, these observations suggest that finger flexion and extension naturally co-occur and that adequate planning of both actions is critical for successful performance, but deficit due to a neurological condition is likely to affect one direction more than the other, suggestive of a biased-overlap hypothesis.

Exertion of force with one or more digits tends to produce unintentional lesser forces in the other digits (i.e., enslaving).^{20–22} Enslaving is essentially the inverse of individuation; lesser enslaving corresponds to greater finger individuation. Our baseline data showed no significant differences in enslaving between the flexion and extension directions. This result contradicts previous reports showing that enslaving is higher during production of extension forces.^{7,15} One explanation might be related to hand orientation during task performance. In most previous studies

the hand was in the prone position, while in our setup it was in a neutral position. Previous work showed that hand posture has a significant effect on the excitability of corticospinal output, and we speculate that this may affect enslaving across orientations.^{23–27} Also, our participants produced much lower instructed finger forces compared with previous work, potentially due to the altered orientation. Indeed, uninstructed finger enslaving increases with increasing instructed finger force.²⁸

The learning curves during the 3-day training (Figure 3) show that both groups had trends of improvement, although the flexor group consistently performed better across dexterity metrics. Improvements were evident within a single day of training, as well as over the 3 training days (Figure 3). The three dexterity measures unveiled the differences in their contribution to overall improvement. Although all dexterity parameters improved, force control and accuracy improved the most.

In the temporal realm, both RT and synchronization improved following training. Improvement in finger dexterity measures within multiday training on multi-finger motor skill was seen previously,²⁹ yet it was specific to the flexion direction. In that study, multiday training led to reduced deviation (e.g., combined metric of force control of the instructed finger and enslaving of uninstructed fingers), faster RT responses and rapid execution times in the flexion direction (the only tested direction). Interestingly, Waters-Metenier et al.²⁹ showed that these dexterity components were augmented if bihemispheric anodal transcranial direct current stimulation (tDCS) was applied to M1 during training, suggesting potential involvement of the motor cortex in the control process of some aspects of finger dexterity. A study that trained participants on a subset of multi-finger chords in the flexion direction found significant generalization in RT and accuracy for chords composed of novel configurations of the practiced elements (i.e., fingers), and chords that contained a new element.³⁰ Our study goes beyond these works, showing that despite the inferior dexterity in extension at baseline, multiday extension-based training improved individuation, force control, and synchronization in the trained direction. The lack of correlation (Figure S5) between the changes in dexterity

components following training indicates that they might be derived from dissociable mechanisms, although our results cannot ultimately confirm this. Of special note is that we established that the reported results are attributed to the generalization effect and not to re-exposure to the test for the second time, or passage of time between baseline and post-training tests.

Our dexterity task can be considered a skill-learning task in which both accuracy and timing parameters are subject to improvement with practice. Evidence indicates that motor skill improvements can be achieved through within-session learning (online effects) and/or between-session learning (offline effects) via consolidation processes.^{31–33} Calculation of online and offline gains (see Figure S6) clearly revealed that across all parameters (i.e., deviation of instructed and uninstructed fingers and temporal synchronization) of both groups, dexterity learning advantages emerged primarily within, rather than between, training sessions.

Direction-dependent generalization of finger dexterity

Our second primary aim was to evaluate generalization of skill improvement between flexion and extension directions within the trained hand. Each group trained on multi-finger chords that required quick, synchronized production of difficult flexor or extensor hand muscle activation patterns, depending on group type.

The context in which an individual trains is known to affect whether learning generalizes to untrained movements.^{3,34,35} Here, the direction of movement (e.g., extension) could be considered the learning context. Both finger flexion and extension movements are strictly context-dependent as each engages separate groups of muscles with distinct activity patterns. Thus, testing the opposite untrained direction constitutes testing generalization to a novel context. We found that transfer across contexts was direction-specific, with learning of extension movement affecting flexion, but not vice versa. The asymmetry between the groups can also be seen in the changes in *II* before and after training. Though both groups had significant improvements in their trained hand and direction, only the extensor group had significant improvement in the opposite direction of the same hand.

The asymmetrical generalization pattern supports a refinement of the partially shared hypothesis when considering the control hypotheses introduced earlier, and thus we propose the *biased-overlap hypothesis*. We interpret this direction specificity, or asymmetry, as a reflection of the differences in neural substrate of the underlying flexion versus extension dexterity. Previous work has exhibited evidence for flexion bias.^{7–14} Nevertheless, interpretation of this result should be treated carefully because change in direction not only changes the context but also the force level needed during flexion vs. extension. Thus, it cannot be concluded that the asymmetrical generalization effect is purely a contextual direction effect.

Some evidence exists supporting the notion that task difficulty might influence amount of generalization. This framework proposes that generalization, or transfer, from a hard to easy task seems to be greater than from an easy to hard task.^{36–39} Since finger extension might be considered a more difficult task than

flexion, it is plausible that our generalization result might be driven by differences in task difficulty. Our analysis, however, ruled this out, showing that although there is a slight difference in difficulty, it is not sufficient to affect the generalization trends.

Lateral, across-hand, generalization of finger dexterity

Learning does not only transfer across direction within the trained hand, but also to the untrained hand. The flexor group had significant improvement in the trained direction in the opposite hand, whereas the extensor group did not. Interestingly, the extensor group improved in untrained hand flexion, which could theoretically be the lateral reflection of the directional generalization discussed earlier. The flexor group, which did not improve in trained hand extension, also did not demonstrate improvement in untrained hand extension. Neither group showed significant improvement in untrained extension.

Flexion-specific generalization to the untrained hand was previously reported in healthy naïve participants^{29,30,40} and stroke patients.⁴¹ For example, we previously found that intensive 5-day training of the paretic hand in a multi-finger task in chronic stroke patients improved finger individuation not only in the trained hand but also generalized to the untrained, non-paretic hand, and lasted for at least 6 months following training.⁴¹ Consistently, other aspects of finger dexterity including force accuracy and reaction times were also generalized to the flexion direction of the untrained hand. This effect was further enhanced if training was coupled with bihemispheric tDCS over M1, suggesting effector-independent representations of dexterity that allowed, in part, intermanual transfer that benefited both hands.²⁹ One explanation of the generalization to the flexion direction of the untrained hand might be attributed to role of the ipsilateral hemisphere during unimanual hand training. Previous neuroimaging studies have consistently observed ipsilateral activation in the sensorimotor cortex. Many of these studies used a sequential finger opposition movement,^{42,43} while others used complex and sequential movements and reported even larger increased activation in ipsilateral parietal and premotor regions.^{30,44} It is possible to think that the ipsilateral hemisphere may contribute to rapid selection of learned sensorimotor associations, and this involvement is especially operated during complex actions as in our multi-finger dexterity training.^{45,46} In a series of experimental conditions, Hazeltine et al.^{30,44} conveniently showed that the strong ipsilateral activity in the left motor cortex was specific to execution of complex movements independent of the sequential nature of the task.

While this interpretation might explain the generalization effect we observed in the flexion direction of the untrained hand, it cannot explain lack of generalization to extension of the untrained hand. The complexity and task demands were similar across directions but generalization to the untrained hand was specific to the flexion direction only. One explanation for the direction-specific generalization across hands might lie in the fact that ipsilateral activation during unimanual movement might be sensitive, not only to task complexity demand, but also to other high-level parameters such as movement direction and/or amplitude,^{47–49} and that this direction-sensitivity is biased more toward flexion. An alternative explanation of the lack of generalization of extension movement might be that these movements

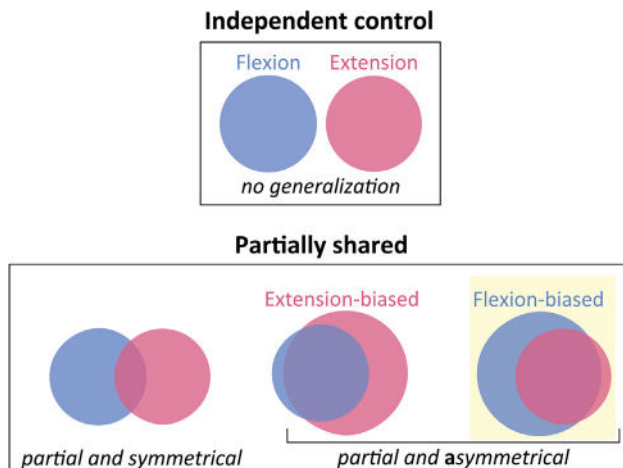


Figure 7. Distinct types of control patterns and associated prediction of generalization of each process

Our data support the interactive flexion-biased overlap relationship between controlling finger flexion and extension of dexterous movement.

are less frequently used in daily function and therefore are less represented in the motor cortex. The structure of activation patterns is determined by the way we use our hands in everyday life.^{50,51} Using functional magnetic resonance imaging (fMRI) paradigms, Ejaz et al.⁵¹ found that frequently co-occurring finger movements in the flexion direction led to strong associations between the cortical modules that encode them. Since extension-based movement is less frequent in our daily function, we speculate that the cortical association of these movements might be less represented compared with flexion. In addition, using direct electrical stimulation over the human motor cortex, flexion of the fingers was evoked far more often than extension.¹⁴ One interpretation for the greater flexion representation is that almost all hand functions, namely grasping objects and using tools, require strong and/or precise finger flexion, with extension being used simply to release or withdraw the fingers.⁵²

In the field of motor behavior, task difficulty can be defined as the level of challenge to execute a motor task within the spatial and temporal constraints.³⁶ Thus, difficulty of a motor task could represent information required to resolve uncertainty of a movement response.^{53,54} Higher values of task difficulty might indicate that more information is needed to choose a correct response from a set of solutions. This increase in information is reflected by longer movement times in tasks with higher difficulty values.^{53–55} When a task becomes increasingly difficult, heightened motor and cognitive demands might act as a stimulus for motor skill learning until processing capacities are exceeded.³⁸ Indeed, it was shown that task difficulty might affect not only performance of the task, but also retention of what has been learned. Retention in younger adults was maximized after practice at the highest of four difficulty levels of a keypress sequence⁵⁶ and the second highest of four difficulty levels of a postural control task.⁵⁷ In our experiment, it is possible that the asymmetrical direction-dependent generalization can be attributed to difference in difficulty between flexion and extension tasks, in which the extension direction might be considered

more difficult and thus learned, retained, and generalized more than flexion. Nevertheless, the lack of significant correlation between task difficulty and generalization of finger dexterity supports our main conclusion of asymmetric and interactive control for multi-finger flexion and extension dexterous movements.

Limitations of the study

An additional explanation for the learning generalization effect may be related to the perceptual and motor representations. Perceptual learning may involve becoming more skilled at recognizing complex patterns formed by the arrays of force targets that define the stimuli patterns,^{58–60} regardless of the movement direction. Motor learning might involve becoming more adept in producing particular multi-finger chord responses. It is also possible that training leads to both perceptual and motor improvements, or those due to specific input patterns being associated with particular chord responses. However, the perceptual stimulus-response hypothesis is unlikely to account for the observed asymmetrical generalization, since both flexion and extension actions required responses to similar stimuli, yet the motor behavior was different. In agreement with the response-based hypothesis, previous work showed that participants were faster in responding to novel stimuli that mapped to practiced multi-finger chord responses compared with those mapped to unpracticed chord responses, suggesting that the learning was largely response based.³⁰

In addition, differences in cognitive demand between flexion and extension tasks, technical aspects of the ergonomic measurement device (e.g., maximal hand size and force capability), specific cognitive processes (e.g., familiarization with the setup and development of strategies during task learning), despite the assumption that they would have equally affected performance regardless of type and direction of action, and muscular fatigue,⁶¹ despite providing breaks between blocks and training at relatively low forces of 25% MVF, all could have had some impact on the dexterity measures. Future work is needed to assess the precise impact of these factors.

Summary and conclusions

The evidence that generalization across directions can occur following unidirectional training supports that control mechanisms of flexion and extension motions are intrinsically connected. When considering this, as well as cortical organization of flexor and extensor motor neurons from previous work, the *independent control* hypothesis does not seem an appropriate control framework of finger dexterity (Figure 7, leftmost panel). One informative direct way to gain insight into the proper functioning of a control system is to monitor its behavior when specific parts of it are affected by illness or injury. The asymmetry between flexion and extension ability and control has been described in numerous stroke studies^{11,12,41} and in animal models with induced brain lesions.¹⁰ The results of this study further corroborate the stark asymmetry between improvements following flexion training and extension training, suggesting a directional dependency that is biased toward improvement in flexion. Therefore, we propose the refined partially shared hypothesis, namely the flexion-biased overlap control hypothesis (Figure 7, most right panel), which appears to adequately reflect

the control mechanism governing single- and multi-finger dexterous movement.

The current study characterizes the behavioral principles underlying the control process, learning, and generalization of dexterous flexion and extension movements. Our data indicate that control of multi-digit dexterous patterns is direction-specific in humans, leading to an alternative biased-overlap hypothesis by which the control circuits for learning of finger flexion and extension are overlapped in that they partially, but asymmetrically, transfer between directions and hands. These findings can be used in future studies, as well as in clinical settings such as rehabilitation protocols for those with unilateral or unidirectional hemiparesis stemming from neural impairments.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.celrep.2023.112214>.

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AUTHOR CONTRIBUTIONS

Conceptualization, G.K., D.S.A., and F.M.; methodology, G.K., O.R., and F.M.; investigation, G.K.; writing – original draft, G.K., D.S.A., and F.M.; writing – review & editing, G.K., D.S.A., and F.M.; funding acquisition, F.M.; supervision, F.M.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Deposited data		
Behavioral data for this study	This study	https://github.com/FirasMawase/Asymmetric-generalization-of-finger-dexterity/tree/main/Data
Code used in this study	This study	https://github.com/FirasMawase/Asymmetric-generalization-of-finger-dexterity/tree/main/Code
Software and algorithms		
Matlab 2020b	The MathWorks, Inc., Natick, MA	https://www.mathworks.com/
GraphPad Prism 9	GraphPad, Dotmatics	https://www.graphpad.com/

RESOURCE AVAILABILITY

Lead contact

Further information and requests should be directed to and will be fulfilled by the lead contact, Firas Mawase (mawasef@bm.technion.ac.il).

Materials availability

This study did not use or generate any reagents.

Data and code availability

All the behavioral data and code to run the experiment are publicly available at <https://doi.org/10.5281/zenodo.7572477>. Any additional information required to reanalyze the data reported in this work paper is available from the [lead contact](#) upon request.

EXPERIMENTAL MODEL AND SUBJECT DETAILS

Subjects

In total, 41 right-handed participants (27 female), aged 25.8 ± 3.7 years (mean \pm STD), were recruited and given monetary compensation for their participation ($300 \text{ min} \approx \90). Participants' handedness was evaluated using the Edinburgh Handedness Inventory 10 item version.⁶² All participants were deemed fully capable in terms of motor abilities, with no history of brain damage or motor impairments affecting finger movements. Naïve participants, with no musical history, were divided into 3 separate groups based on the trained direction (flexor vs. extensor): Flexor group ($n=13$) who trained on finger flexion, Extensor group ($n=13$) who trained on finger extension, and a control group ($n=12$) which performed two testing sessions 4 days apart, without undertaking training in between the tests. A participant with no musical history was considered as if she/he has less than six consecutive months of formal and/or informal musical training. Three participants were excluded from analysis due to incomplete or missing data, drop out or inability to learn the task.

METHOD DETAILS

User interface and data acquisition

During the study, participants placed both hands in a neutral posture inside an adjustable ergonomic device that measured isometric finger forces, with a force sensor (FSG-02OWNPB, Honeywell®; dynamic range 0–20 N) below each fingertip to measure flexion forces and a sensor above each fingertip to measure extension forces (see [Figure 1A](#) in the main text). Analog force signals were digitized and sampled at 250 Hz (using NI USB-6211 data acquisition), and then integrated with a customized MATLAB script (The MathWorks, Inc., Natick, MA, ver. R2020b) enabling live measurements, presentation, and analysis. Using Psychtoolbox,⁶³ visual stimuli presented on a computer screen signaled the participants which fingers were required to move and at what force. The target forces were normalized to 25, 50, and 75% of each participant's maximum voluntary force (MVF) for each finger.

During testing and training, participants were instructed to move only the relevant fingers to the appropriate target forces while maintaining the uninstructed fingers at rest. A force tolerance around each target force represented the target zone in green, whereas uninstructed fingers had a red zone of $\pm 5\%$ MVF around 0 N. For example, [Figure 1B](#) in the main text shows a trial in which participants were instructed to extend their thumb and index fingers to 25% of MVF while maintaining the uninstructed fingers immobile.

Participants were incentivized with a point and a success sound when they completed a trial correctly (i.e., all instructed fingers were within the green zones and all uninstructed fingers were within the red zone). Points were aggregated during each block and the total point count from all blocks was displayed at the end of each block. Participants were explicitly told that this feedback is not related to the compensation for their participation in the experiment.

Study design

The primary aim of this study was to characterize the learning and generalization of finger dexterity in the flexion and extension directions. Therefore, two different cohorts of participants (Flexor and Extensor) were trained with the dominant right hand over three sessions (days 2–4), in the flexion or extension direction, respectively. We first quantified the learning effect in multiple dexterity measures within the trained direction. We then quantified the generalization of learning effects to the untrained direction (directional generalization) and to the untrained hand (lateral generalization) during the post-training tests conducted after training (on day 5). An additional group of participants was used as a control group which did not partake in training but only performed the tests on day 1 and day 5.

More specifically, the study spanned 5 consecutive days (see Figure 1C in the main text). On the first day (pre-training), the participants' MVF and baseline measurements were acquired. On days 2, 3, and 4 the participants performed the training according to their group type. On the fifth day (post-training), the participants underwent the same measurements as on the first day. **Day 1 (pre-training)** – Following an explanation of the visual stimuli and a short demonstration of the hand sensors, the hand device was adjusted according to the participants' hand dimensions. The MVF of each finger was obtained using the 'Finger strength task' (Figure 1B). Next, initial baseline measurements were obtained using the 'Individuation and chord testing task'. **Day 2, 3, 4** – Participants performed the 'Training task', according to their group type. **Day 5 (post-training)** – Participants performed the 'Individuation and chord testing task', as in day 1, and received compensation for their participation.

Trial and block design

The study was built in a trial and block design. Each session was separated into multiple blocks, which contained multiple trials that occurred one after another automatically. In order to reduce fatigue, each block was started manually so participants could remove their hands from the devices between blocks. Each trial in the testing and training tasks consisted of the same procedure: The GUI signaled which finger is to move 750 ms prior to displaying the green target zones, and participants had 5 seconds to successfully enter the green zones. If reached, participants were instructed to hold the force and stay within the green zone for two seconds. If all instructed fingers were within the green zones and all the uninstructed fingers were within the red zones, then the trial was considered successful, and the participants were awarded with a point and a 'success' tone. The next trial began automatically after 250 ms (inter-trial interval, ITI).

Finger strength, individuation and chord testing, and training tasks

All tasks were performed when the participant was seated facing a computer screen with both hands inside the hand devices. Participants could remove their hands from the device between blocks. Prior to the beginning of each task, participants were provided with an overview of the task and its requirements. The tasks used are similar to those used in previous works.^{41,64} In order to accurately measure the isometric forces during activity while considering forces produced by the hands' placement and finger weights, we subtracted forces measured by the sensors while participants were in a neutral position and at rest. This zeroing procedure was performed before each block and at multiple times throughout the experiment.

Finger strength task

This was the first task performed by each participant in order to find the MVF of each finger in each direction. During each trial, participants were asked to produce as much force as they could in a certain finger and in a certain direction and maintain that force for three seconds (Figure 1B, left panel). Here, participants were not limited to using only the instructed finger to produce the maximal force. Due to limitations in the force capability of the sensors, participants were allowed to produce forces up to 14 N. If the force produced exceeded 14 N, then the green target zone turned red, and participants were asked to reduce their force slightly. Forces larger than 14 N mainly occurred during thumb and index flexion, if at all, so this limitation did not affect all participants nor all MVF values.

The order in which the MVF values were measured was right hand (RH) flexion, RH extension, left hand (LH) flexion, and LH extension, in order from thumb to little finger. The maximum force of each trial was calculated as the 95th percentile of the finger's force data for the trial. Each movement performed twice and the maximum between the two repetitions was selected as the relevant MVF value.

Single finger individuation and multi-finger chord tasks

This task was performed on the first and last day of the study, to provide the baseline (pre-training) and final (post-training) learning abilities, respectively. Participants were instructed to move only the instructed finger(s) while maintaining the other fingers at rest. This task consisted of 388 trials in 8 separate blocks, each of which tested a different subgroup of movement: RH Individuation - Flexion, RH Individuation - Extension, LH Individuation - Flexion, LH Individuation - Extension, RH Chords - Flexion, RH Chords - Extension, LH Chords - Flexion, and LH Chords - Extension.

The individuation blocks consisted of 3 repetitions of three force levels (25%, 50%, and 75% of MVF) for each finger, totaling at 45 trials per block. Trials were performed in order from thumb to little finger. The chord blocks consisted of two repetitions of the 25%

force level in the remaining 26 finger combinations (i.e., 31 a total of 31 possible combinations in one hand including, 5 single finger movements and 26 multiple finger combination), totaling at 52 trials per block. The chord order was based on a similar organizational scheme as the single finger trials (thumb to little finger), starting with 2-finger combinations, then 3- and 4- finger combinations, and finally all five fingers. For example, the 2-finger combinations started with thumb and index and went to thumb and little, and then index and middle to index and little, etc. All 3- and 4- finger combinations were organized similarly. The force tolerance around each target force was set at 10% of MVF. This task took roughly 60-75 minutes to complete. Participants of all groups performed identical pre- and post-training tests.

Training task

The training task was performed on days 2,3 and 4 of the study and included a total of 310 trials in 5 blocks. Each block contained two repetitions of all 31 finger combinations at the 25% force level, presented in a random order. Training was done only on the right hand. The direction of the training depended on the group the participant belonged to: 'Flexors' trained in the flexion direction and 'Extensors' trained in the extension direction. The force tolerance around the target forces decreased by 85% per day (8.5%, 7.2%, and 6.1% of MVF, respectively). This task took roughly 50-60 minutes to complete. Participants in the control group did not perform these training days.

QUANTIFICATION AND STATISTICAL ANALYSIS

Measurable metrics

Prior to extracting metrics from the raw data, various preprocessing analyses were implemented: (1) *low-pass filtering*, the force data of each sensor was filtered using a gaussian filter (over a 16 ms time window) to eliminate the electrical noise from the sensors. (2) *baseline-correction*, the forces present at the beginning of each trial (baseline forces) were calculated over the initial 1.5 seconds of the trial in three segments (0-0.5, 0.5-1.0, 1.0-1.5 seconds). In order to verify that the finger was at rest, the standard deviation of each segment was calculated. If the standard deviation of the segment with the lowest standard deviation was less than 0.2, then the mean force of that segment was chosen as the baseline force. The baseline forces, if available, were then subtracted from the data, resulting in modified forces which start at 0N for each trial. Sample processed trial data of single finger movement can be seen in Figure 2B in the main text, and sample processed trial data of multi-finger movement can be seen in Figure 2C. Following the preprocessing stage, the global maximum force of each instructed finger was found and was used to find the movement onset and end times. The onset and offset timestamps were classified as the first and last times the force passed 50% of the global maximum force, respectively. If there was more than one instructed finger, the longest range was selected (see onset times in Figure 2F in the main text).

Individuation index (II)

One of the main components of finger dexterity is the ability to individuate our fingers. In order to quantify this ability and test how it altered and potentially generalized following training, a metric called Individuation Index (II) was calculated and compared over the duration of the study.⁶⁴ The II describes the relationship between the forces generated by the instructed finger and the uninstructed fingers. The II was derived from the mean deviations of the uninstructed fingers and the peak force of the instructed finger in each specific trial. The mean deviation of the uninstructed fingers (*meanDevU*) was calculated using the following equation:

$$meanDevU = \frac{1}{T} \sum_{t=0}^T \sqrt{\sum_{j=uninstructed} (F_{t,j})^2}$$

where the index *j* denotes the *j*th uninstructed finger, *T* and *t* represent time, *F*_{*t,j*} is the *j*th finger's force level at time *t*, and the deviation was calculated from *F*=0N. The timespan evaluated for this calculation was between the movement onset and end times (see arrow in Figure 2C). The peak force and mean deviation values of the various trials for the same finger present a positive linear relationship, with increasing uninstructed finger deviation for increased peak instructed finger force. The II of each finger was calculated as the negative log of the slope, and the II of each hand was the average of the finger II values (see Figure 2D in the main text). The higher the II value, the better the individuation ability.

Force control of the instructed fingers

Dexterity can be also described in terms of force accuracy of the instructed fingers. The ability to generate accurate force of the instructed finger(s) was quantified by measures of deviation from the target (i.e., *meanDevI*), using the following equation:

$$meanDevI = \frac{1}{T} \sum_{t=0}^T \sqrt{\sum_{i=instructed} (F_{t,i} - (TF - BF))^2}$$

where the index *i* denotes the *i*th instructed finger, *T* and *t* represent time, *F*_{*t,i*} is the *i*th finger's force level at time *t*, *TF* is the pre-defined target force, and *BF* is the baseline force calculated during the preprocessing stage. The timeframe for the calculation was the movement onset and offset times as defined previously (see pink and orange regions in Figure 2C in the main text).

Temporal synchronization

In the time domain, one of the main principles underlying the control process of multi-finger dexterous movements is how participants synchronize their force patterns when presented with targets incorporating multiple fingers. Synchronization is defined as the

temporal alignment between active fingers and is calculated as variance (e.g., standard deviation) of the response, or reaction time (RT), of the instructed fingers. Low RT variability indicates enhanced synchronization between the instructed fingers (right panel, [Figure 2F](#) in the main text), whereas high variability indicates reduced synchronization (left panel, [Figure 2F](#) in the main text). RT of each finger is defined as the time interval between the “Go” cue and the force initiation (detected as the time in which the force signal crossed the threshold of 10% of peak force). In chord targets, the overall RT was considered the reaction of the first finger to surpass the 10% threshold.

Task difficulty

Task difficulty during learning might also affect subsequent generalization. In the perceptual and motor learning literature, it was found that the difficulty of a task affects expected performance during learning, the potential information arising from performance, and the amount of generalization thereafter. Based on this framework, it is expected that transfer from a hard task to an easy task is greater than from an easy to a hard task.^{38,39} For example, in a reaching task where difficulty was defined as distance to the target, and transfer was defined as performance on a target not included in the acquisition phase, it was found that high nominal task difficulty in practice benefitted single-task transfer persistence.^{36,37}

Therefore, it is plausible to speculate that since finger extension (compared to finger flexion) induces greater difficulty during training, extension might lead to greater generalization over the two directions. To test this concept in the realm of our task, we first defined the difficulty space in our task as the space of execution time and deviation of the instructed fingers (i.e., inverse to accuracy) in day 1 (i.e., baseline session) ([Figure 6A](#) in the main text). In this difficulty space, finger chords with increased execution time and increased deviation were considered difficult chords while chords with short execution time and low deviation (i.e., increased accuracy) were considered to be less difficult chords. We mapped all chords in both the flexion and extension direction within this space and defined three different levels of difficulty based on the distance from the origin: Low ($distance \leq 33.33\%$), Mid ($33.33\% < distance \leq 66.67\%$) and High ($distance > 66.67\%$). We then directly tested whether the difference in difficulty between the flexion and extension task affected the generalization.

Statistical analysis

The statistical analysis was performed using Matlab software (MathWorks) and Prism software (GraphPad). To determine the effect of learning in force control (i.e., deviation of the instructed fingers), enslaving (i.e., deviation of the uninstructed fingers) and synchronization, we performed for each group (Flexor and Extensor) two-tailed paired t-tests between the first block of the training (i.e., day 2) and the last block of the training (i.e., day 4). To determine the across-direction generalization, we then used separate (for each group) 2-way repeated-measures ANOVA (2-way RM-ANOVA) to assess differences in individuation index, force control, and synchronization of the trained hand, with factors of time (pre vs. post training) and direction (flexion vs. extension). For across-hand generalization statistics, we also used separate 2-way RM-ANOVA with factors of time (pre vs. post training) and direction (flexion vs. extension). For the difficulty effect statistic, we used 2-way RM-ANOVA on the improvement (post-pre) of enslaving (i.e., $meanDevU$) with factors of chord difficulty (low, mid, high) and group (flexor vs. extensor) for each direction. When significant differences were identified, post hoc analysis was conducted using the Holm-Šidák paired t-test for correcting multiple comparisons. In all comparisons, the significance level was set at 0.05. Additionally, we performed ANCOVA to test for effect of baseline differences between the flexion-trained group and the extension-trained group in our data.