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External biomechanical constraints impair maximal voluntary grip force stability post-stroke

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ABSTRACT

Background: Grip strength is frequently measured as a global indicator of motor function. In clinical populations, such as hemiparesis post-stroke, grip strength is associated with upper-extremity motor impairment, function, and ability to execute activities of daily living. However, biomechanical configuration of the distal arm and hand may influence the magnitude and stability of maximal voluntary grip force and varies across studies. The influence of distal arm/hand biomechanical configuration on grip force remains unclear. Here we investigated how biomechanical configuration of the distal arm/hand influence the magnitude and trial-to-trial variability of maximal grip force performed in similar positions with variations in external constraint.
Methods: We studied three groups of 20 individuals: healthy young, healthy older, and individuals post-stroke. We tested maximal voluntary grip force in 4 conditions: 1: self-determined/“free”; 2: standard; 3: fixed arm-rest; 4: gripper fixed to arm-rest, using an instrumented grip dynamometer in both dominant/non-dominant and non-paretic/paretic hands.
Findings: Regardless of hand or group, maximal voluntary grip force was highest when the distal limb was most constrained (i.e., Condition 4), followed by the least constrained (i.e., Condition 1) (Cohen's $f = 0.52$, *P*'s < 0.001). Coefficient of variation among three trials was greater in the paretic hand compared with healthy individuals, particularly in more (Conditions 3 and 4) compared to less (Conditions 1 and 2) constrained conditions (Cohen's $f = 0.29$, *P*'s < 0.05).
Interpretation: These findings have important implications for design of rehabilitation interventions and devices. Particularly in individuals post-stroke, external biomechanical constraints increase maximal voluntary grip force variability while fewer biomechanical constraints yield more stable performance.

1. Introduction

Grip force is a robust measure of normal human motor function (Nasreddine et al., 2005), only in part because the ability to generate adequate grip force is critical to performance of activities of daily living (ADL) (de Freitas and Lima, 2013). Due to its ubiquity, grip strength is a common clinical measurement, often used as a proxy for health status across the lifespan (Nasreddine et al., 2005; Shechtman, 2000). Even post-stroke, grip strength is strongly associated with overall upper extremity (UE) function (Boissy et al., 1999), independence in ADL (Bae et al., 2015), and has been suggested as a global representation of UE weakness (Ekstrand et al., 2016).

Production of maximal voluntary grip force (MVGF) is influenced by both neural and biomechanical factors. Due to stroke-related disruption of the corticospinal tract and indirect descending motor pathways, paretic hand MVGF tends to be reduced and less stable (Kang and Cauraugh, 2015). Stability of MVGF can be measured by motor output variability, including both variability within-a-trial and trial-to-trial variability (Christou and Tracy, 2006). Within-a-trial force variability has been widely studied during sustained submaximal power grip post-stroke, leading to the current assertion that paretic hand grip force is less stable than in healthy adults (Chang et al., 2013; Lindberg et al., 2012; Lodha et al., 2010). Related to within-a-trial variability, trial-to-trial variability is also an important component of motor output variability reflecting the ability to produce consistent, reproducible motor activity (Christou and Tracy, 2006; Shechtman, 2000). In older adults increased trial-to-trial variability of peak force is observed more frequently than within-a-trial variability (Christou and Tracy, 2006)

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suggesting it affords greater sensitivity for detecting age-related motor control deficits than within-a-trial variability. Observation of such differences with aging provides rationale for investigating trial-to-trial variability of maximal power grip to detect and understand motor control deficits post-stroke. Trial-to-trial variability of maximal power grip has not been systematically investigated in the post-stroke population.

Overall arm posture and biomechanical configuration of the distal arm/hand are two factors that influence MVGF production. Previous studies suggest that both proximal (Dominici et al., 2005; Ginanneschi et al., 2005, 2006; Su et al., 1994) and distal (Komi, 1974; Odriscoll et al., 1992) arm position can influence MVGF magnitude. To eliminate these biomechanical influences and enable generalizability of results across studies (Roberts et al., 2011), the American Society of Hand Therapists (ASHT) has recommended a 'standard position' (i.e., shoulder adducted and neutrally rotated, elbow flexed at 90°, forearm neutral, wrist held between 0°–30° dorsiflexion and 0°–15° ulnar deviation) for measurement of MVGF (Fess, 1992).

Different from relatively consistent arm posture, biomechanical configuration of the distal arm during MVGF measurement varies markedly (Brogardh et al., 2015; Choi et al., 2010; Ekstrand et al., 2015; Hamilton et al., 1992; Lariviere et al., 2010; Martins et al., 2015a, 2015b; Massy-Westropp et al., 2011; Mathiowetz et al., 1985; Motawar et al., 2016; Paclet et al., 2014; Persson et al., 2015; Shechtman et al., 2005; Ye et al., 2014). In most studies of healthy adults, participants are instructed to attain the standard arm position and maintain it voluntarily without external biomechanical constraints (Hamilton et al., 1992; Mathiowetz et al., 1985; Shechtman et al., 2005). Notably, many individuals post-stroke have difficulty coordinating the simultaneous tasks of maintaining the standard position, stabilizing the grip dynamometer, and producing MVGF. In addition, due to abnormal flexor synergy patterns (Brunnstrom, 1970; Dewald et al., 1995), individuals post-stroke are likely to produce off-axis movements with the arm and hand during grip (Brunnstrom, 1970; Chae et al., 2002). As a result, some investigators have used external biomechanical constraints to maintain the paretic limb position with the goal of preventing these off-axis movements (Ekstrand et al., 2015; Lodha et al., 2012, 2013; Martins et al., 2015a, 2015b; Persson et al., 2015; Ye et al., 2014). These external constraints take various forms, for example, manual arm stabilization by an experimenter during grip (Martins et al., 2015a, 2015b), placing or strapping the arm on a table or armrest (Ekstrand et al., 2015; Persson et al., 2015; Ye et al., 2014), or fixing the grip dynamometer to the table or apparatus (Lodha et al., 2012, 2013).

How biomechanical configurations of distal arm influence magnitude or between-trial stability of MVGF has not been investigated in healthy individuals or individuals post-stroke. External constraint of the distal arm reduces the degrees of freedom (DoF) (Bernstein, 1967; Bober et al., 1982; Fischer et al., 2009; Kornecki et al., 2001; Seo and Armstrong, 2009), which has been associated with reduced activity in wrist stabilizing muscles (Fischer et al., 2009; Kornecki et al., 2001) and increased activity in primary movers (Kornecki et al., 2001), thus potentially contributing to increased MVGF magnitude. While it is recognized that trial-to-trial variability can be influenced by the presence of neuromuscular impairment and motor task (i.e., task difficulty, the number of joints involved, etc.) (Lechner et al., 1998; Simonsen, 1995; Tornvall, 1963), it remains unclear whether trial-to-trial variability can be influenced by biomechanical configurations of distal arm.

Beyond straightforward variations in MVGF magnitude and between-trial stability, differences in biomechanical configuration alter the motor task (e.g., external constraints requiring the person to adjust to the task vs. unconstrained movements allowing the task to be adjusted to the person). As popular rehabilitation devices, end-effector based robots provide external constraints to the arm, ostensibly to promote focus on training hand function (Dovat et al., 2008; Masia et al., 2007; Oblak et al., 2010). In contrast, exoskeleton robots do not constrain natural joint movements to fixed positions (Balasubramanian et al., 2010). It remains unclear how the contrasting biomechanical configurations of these designs influence neural control of movements performed as part of rehabilitation and which might lead to greater rehabilitation efficacy. Therefore, understanding the influence of biomechanical configurations on motor performance, particularly in the post-stroke population, would inform the design of rehabilitation interventions and devices.

Here we investigated the magnitude and stability of MVGF across four biomechanical configurations with different levels of external constraint in healthy young and older adults, and individuals post-stroke. We hypothesized: (1) MVGF magnitude varies as a function of biomechanical constraint with higher MVGF observed in more constrained conditions; (2) paretic hand MVGF stability is reduced independent of condition; and (3) biomechanical configuration does not influence MVGF stability.

2. Methods

2.1. Subjects

Twenty individuals in the chronic phase post-stroke, twenty young, and twenty older healthy adults participated. Individuals post-stroke meeting the following criteria were included: clinical presentation of a single, mono-hemispheric stroke with resulting hemiparesis of at least 6 months duration able to perform power-grip in the 'standard position' (Fess, 1992), unaccompanied by significant UE joint pain, severe osteoarthritis or prior pathological fracture, or significant cardiovascular impairments contraindicative to exertion. Inclusion criteria for healthy adults were absence of: disease, injury, or prior surgery that could affect UE strength, or presence of UE pain. Demographic characteristics are reported in Table 1.

Each subject provided written, informed consent prior to enrollment and participation. Approval for all procedures was attained from University of Florida Health Science Center Institutional Review Board (IRB-01) and carried out in conformity with the standards set by the Declaration of Helsinki.

2.2. Instrumentation

MVGF was assessed during isometric power grip using a custom grip dynamometer instrumented with a capacitive load cell (iLoad Mini MFD-200 & DQ-1000A, Loadstar Sensors, Fremont, California). Transducer calibration using weights of known mass was linear under both loading and unloading conditions. The grip dynamometer could be adjusted to three positions (i.e., apertures) consistent with standard dimensions of commercially available grip dynamometers; all participants were tested in Position 2 (i.e., aperture length 4.76 cm (Mathiowetz et al., 1985; Trampisch et al., 2012)). Analog signals were sampled (2000 Hz) and processed online (100 ms moving-window median) using Signal (Version 6.0, Cambridge Electronic Designs, Cambridge, UK). Real-time feedback was provided by displaying the processed force signal on a television screen (Samsung, TruSurround HD, Dolby Digital, 48 in.). The maximal value of each filtered force trace was identified in software and recorded as MVGF for statistical analysis.

2.3. Experimental protocol

2.3.1. Clinical assessments

The Edinburgh Handedness Inventory (Oldfield, 1971) was used to determine laterality and the Montreal Cognitive Assessment (MoCA) to characterize cognitive function in all participants (Rossetti et al., 2011). Motor impairment was assessed in individuals post-stroke using the upper-extremity component of the Fugl-Meyer Motor Function Assessment (UE FMA) (Fugl-Meyer et al., 1975) and the Modified Ashworth Scale (Bohannon and Smith, 1987).

Table 1
Participant characteristics.

Characteristics	Individuals post-stroke		Older healthy adults		Young healthy adults	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age (years)	63.4 (10.2)	43–83	61.25 (7.7)	51–80	23.7 (3.4)	20–30
Sex						
Male	17		9		8	
Female	3		11		12	
Handedness (healthy) or premorbid handedness (stroke)						
Right	20		17		16	
Left	0		3		4	
Side affected						
Right	7					
Left	13					
Time since onset of stroke (years)	4.9 (4.1)	0.5–15.6				
UE-FMA (0–66)	53.9 (15)	12–66				
Modified Ashworth Scale (0–5)	0.48 (0.67)	0–2.14				
MoCA (0 – 30)	26.39 (2.91)	20–30	28.65 (1.97)	22–30		

UE-FMA refers to upper-extremity component of the Fugl-Meyer Motor Assessment (Fugl-Meyer et al., 1975). Modified Ashworth Scale (Bohannon and Smith, 1987) reported as group mean (SD) with individual subject scores derived from the average over seven joint movements: shoulder flexion, extension, external rotation, elbow flexion and extension, wrist flexion and extension. MoCA – Montreal Cognitive Assessment – normative scores for 60–70 years of age average 20.89 and 24.32 for those with less than or greater than 12-years' education, respectively (Rossetti et al., 2011). No significant difference in age was revealed between stroke and older adults ($P > 0.05$).

2.3.2. Maximum voluntary grip force

Participants were seated comfortably in a chair throughout the experiment. During MVGF production, participants were instructed to: maintain the position of the gripping limb and dynamometer, squeeze the grip dynamometer "as hard as possible", and "hold" for three seconds. The same verbal encouragement was provided during each grip. Participants were not provided performance feedback (i.e., MVGF value).

2.3.3. Four biomechanical conditions

MVGF was tested in four conditions: C1 'free', C2 'standard', C3 'arm rest', and C4 'fixed' (Fig. 1). In the first condition (C1), participants were handed the grip dynamometer at the standard position (Fess, 1992) and instructed to, "find your preferred position to produce your maximum grip strength." Following the first trial, they were instructed to remember this position for use in subsequent trials. The gripping arm was videotaped during the first trial. During the second and third trials, participants were instructed to reproduce the position used for the first trial and the videotape was used to verify or remind them of their self-determined position. In the second condition (C2), participants were handed the grip dynamometer and verbally instructed to attain each component of the standard position (Fess, 1992). Participants were coached, as necessary, to re-attain the standard position at the beginning of each trial. The third condition (C3), paralleled the standard position, but the forearm was supported by an armrest with the wrist and hand unconstrained. The fourth condition (C4), also maintained standard position with the forearm supported by the armrest, but the grip dynamometer was rigidly fixed at the distal end of the armrest. Thus, across conditions, shoulder and elbow position remained consistent, but constraint of the forearm, wrist, and hand varied.

2.4. Experimental procedure

Both hands were tested in random order. Within each hand three MVGF trials were obtained in each of the four conditions randomized by block. Each trial was followed by a 2-minute rest interval.

2.5. Data analysis

Data were analyzed using SPSS® Statistics (Version 22, IBM Corporation, Armonk, NY). Descriptive statistics (means and standard deviations (SD)) were calculated for participant characteristics and MVGF. The coefficient of variation (CV = SD/mean) was used to measure trial-to-trial variability of MVGF for three repeated trials within each condition by hand for each subject. Proportionality between the mean and SD is a prerequisite to using CV as a measure of variability (Lechner et al., 1998; Portney and Watkins, 1993; Shechtman, 2000). Proportionality between mean and SD of repeated MVGF trials was tested in the full sample (both hands, all participants) using Pearson correlation. Trend analysis (i.e., linear regressions between trial number and MVGF) was conducted to test for systematic effects (e.g., fatigue, learning) across all 12 trials in each hand for each group.

Data were found to meet the normality assumption using the Kolmogorov-Smirnov test. MVGF and CV were analyzed in separate mixed design (Group (3) × Hand (2) × Condition (4)) ANOVAs with repeated measures on the last two factors. Sex was used as a covariate when linearly related to the dependent variable and meeting the homogeneity of regression assumption. Sphericity was tested using Mauchly's test and the Greenhouse-Geisser correction applied when non-sphericity occurred. Bonferroni's correction was applied for multiple comparisons; corrected P-values are reported for post hoc tests. Statistical significance was established at $P < 0.05$.

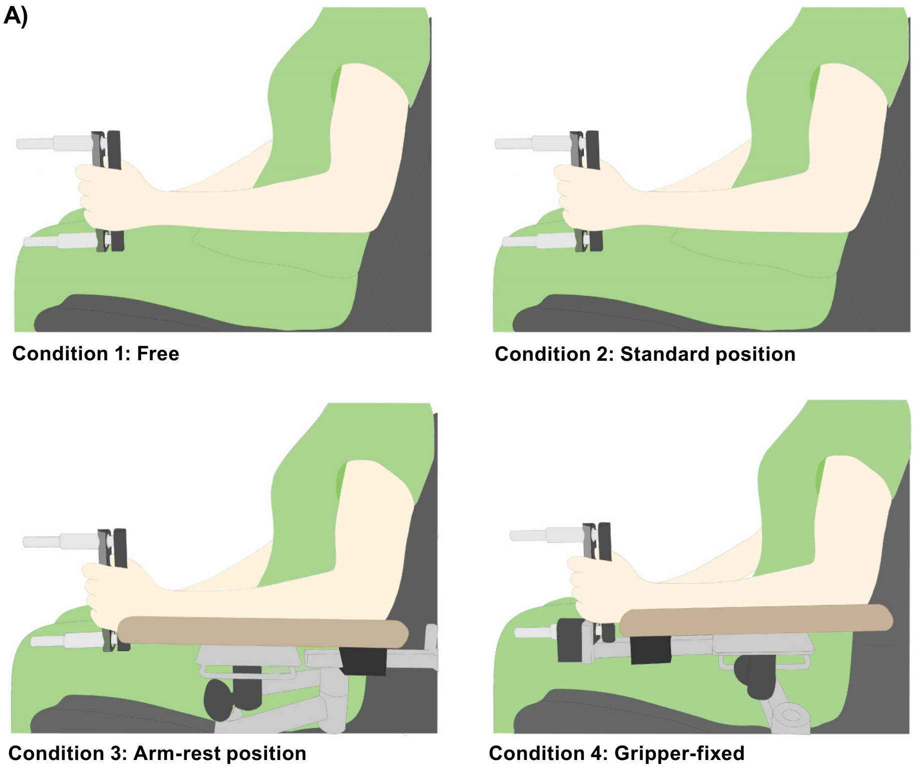
3. Results

3.1. Magnitude of maximum voluntary grip force

Sex was linearly related to MVGF, indicating that males produced significantly higher MVGF than females ($P < 0.001$), thus was used as a covariate in this model. MVGF collapsed across groups and hands revealed a significant main effect of Condition ($F_{2,\ 111.99} = 14.89$, $P < 0.001$). Post hoc testing revealed higher MVGF in C4 than all other conditions (P's < 0.001). MVGF in C1 was also significantly higher than C2 or C3 (P's < 0.001) (Fig. 2).

A significant two-way (Group × Hand) interaction ($F_{2,\ 56} = 17.23$; $P < 0.001$) confirmed the unsurprising result that paretic hand MVGF in individuals post-stroke was significantly lower than either the non-paretic hand or the non-dominant hand of healthy young and older participants (P's < 0.001). Non-paretic hand MVGF in individuals post-stroke was significantly lower than the dominant hand of young participants ($P = 0.048$), but did not differ statistically from the dominant hand of

A)



B)

	C1 free	C2 standard	C3 arm rest	C4 fixed
Shoulder	3	0	0	0
Elbow	1	0-1	0	0
Forearm	1	0-1	0-1	0
Wrist	2	0-2	0-2	0
Total	7	0-4	0-3	0

Fig. 1. Four grip conditions with ostensibly similar biomechanics.
A). Shoulder, elbow, and wrist position were held constant across all four experimental conditions while instructional (C1, C2) and mechanical (C3, C4) constraint of the forearm and wrist were varied.
B). Degrees of Freedom (DoF) by condition: C1, no instructional constraint all upper limb joints allowed full DoF; C2, participants verbally instructed to maintain standard position (described in text and (Fess, 1992)). The upper arm was stabilized by trunk reducing shoulder DoF. Although instructed not to move, elbow, forearm and wrist DoF were not constrained and could vary among participants. C3, forearm supported by an armrest constraining elbow movement but forearm and wrist DoF still allowed and could vary among participants. C4, whole arm constrained by armrest and fixed dynamometer, reducing DoF at all joints.

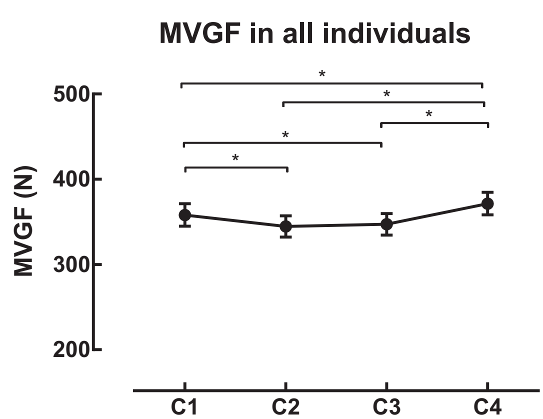


Fig. 2. MVGF magnitude all conditions. Data presented are mean ± SEM, adjusted by sex as covariate. * indicates significant between-condition difference (P's < 0.001). Regardless of hand or group, MVGF magnitude was highest in C4, followed by C1.

older adults. No significant MVGF difference was revealed between dominant and non-dominant hands in either young or older adults. Furthermore, no significant MVGF differences were revealed between healthy older and young adults in either hand (Fig. 3). The overall pattern of MVGF magnitude described above was similar across groups and hands (Fig. 3) as confirmed by absence of significant three-way (Group × Hand × Condition) interaction ($F_{4.38,122.67} = 0.76$, $P > 0.05$).

No significant trend was revealed during the course of experiment in any hand or group (P's > 0.05), indicating the absence of systematic effects of fatigue or learning.

3.2. Between-trial stability of maximum voluntary grip force

The mean and SD of repeated MVGF trials were significantly correlated in both hands of all participants ($R^2 = 0.1$, $P < 0.0001$) thus meeting the prerequisite of proportionality between these parameters to evaluate the CV (Lechner et al., 1998; Portney and Watkins, 1993; Shechtman, 2000). Sex was not significantly correlated with CV ($P > 0.05$), thus was not included in this statistical model as a covariate. A significant three-way (Group × Hand × Condition) interaction ($F_{5,142.56} = 2.463$; $P = 0.036$) revealed greater CV in the paretic relative to the non-paretic, hand of individuals post-stroke in all four

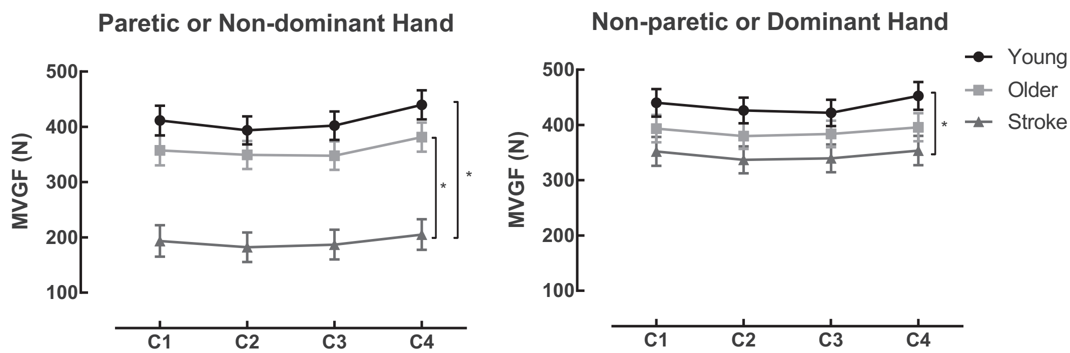


Fig. 3. MVGF magnitude by group and hand. Data presented are mean ± SEM, adjusted for covariate of sex. MVGF was significantly lower in the paretic hand of individuals post-stroke than the non-paretic hand and the non-dominant hand of healthy young and older participants. MVGF was also significantly lower in the non-paretic hand of individuals post-stroke than the dominant hand of healthy young participants. No MVGF difference was revealed between dominant and non-dominant hands and age groups in healthy participants.

conditions ($P < 0.001$) (Fig. 4), both hands of healthy older participants, the dominant hand of healthy young participants (all four conditions, P's < 0.05), and the non-dominant hand of healthy young participants in C3 and C4 (P's $= 0.004$ and 0.001). Within the paretic hand of individuals following stroke, CV was higher in C3 than C1 ($P = 0.046$), and C4 was higher than C1 and C2 (P's $= 0.034$ and 0.047) (Fig. 4). No significant differences in CV were detected across conditions in the non-paretic hand of stroke or the dominant hand of healthy participants (Fig. 4). Mean paretic hand MVGF and SD, by condition, are illustrated in Fig. 5.

4. Discussion

This study investigated how external biomechanical constraints of the distal arm influence magnitude and stability of MVGF. This is the first study to directly compare MVGF across conditions with varied external biomechanical constraints in healthy young and older adults and stroke populations. Our primary findings are: (1) MVGF magnitude is highest when the distal limb is most constrained (i.e., fixed gripper) – regardless of hand or group – followed by the least constrained condition (i.e., 'free'); (2) MVGF stability between-trials is reduced in the paretic hand of individuals post-stroke compared with healthy participants; and (3) contrary to our hypothesis, MVGF stability in the paretic hand of individuals post-stroke is reduced in the presence of increased biomechanical constraints.

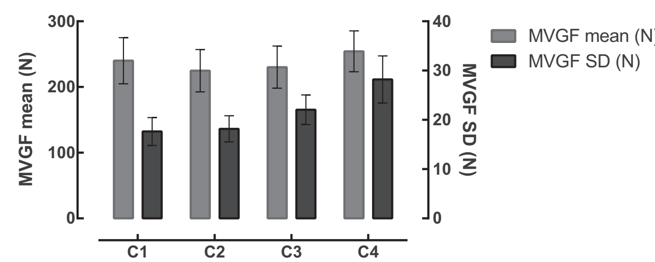


Fig. 5. Mean paretic hand MVGF and SD by condition. MVGF magnitude varies, somewhat, across conditions while SD increases monotonically from C1 to C4. Greater CV in C3 and C4 can be attributed to increased variability rather than reduced MVGF magnitude. Data presented from only paretic hand of persons post-stroke for sake of illustration.

4.1. *MVGF magnitude is highest in the most constrained, followed by the least constrained, condition*

Other authors have measured MVGF with either free or fixed dynamometer configurations (Brogardh et al., 2015; Choi et al., 2010; Ekstrand et al., 2015; Hamilton et al., 1992; Lariviere et al., 2010; Martins et al., 2015a, 2015b; Massy-Westropp et al., 2011; Mathiowetz et al., 1985; Motawar et al., 2016; Paclet et al., 2014; Persson et al., 2015; Shechtman et al., 2005; Ye et al., 2014), but direct comparison of the effects of biomechanical constraint on MVGF magnitude across more than two conditions has not been reported previously. Independent of group or hand, we observed the highest MVGF magnitude

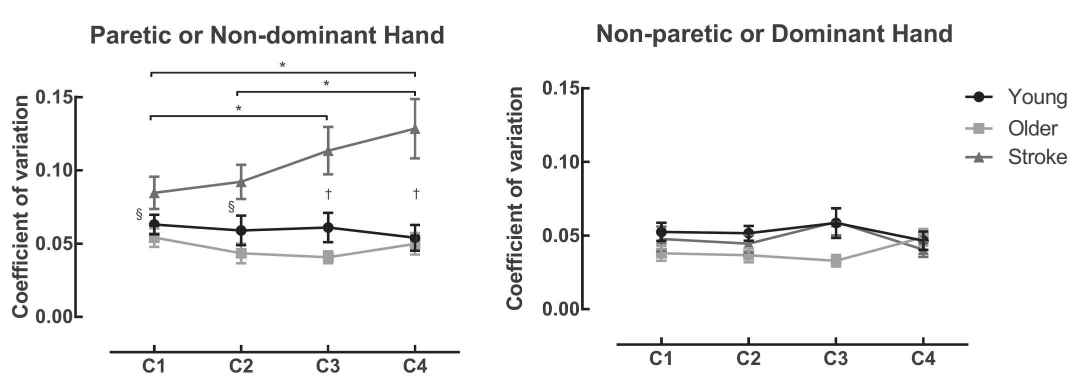


Fig. 4. CV of MVGF by group, hand and condition. Paretic hand MVGF stability is systematically reduced with external biomechanical constraints. Overall CV in the paretic hand of persons post-stroke is greater than the non-paretic hand and both hands of healthy participants, especially in C3 and C4. Within the paretic hand, CV in more constrained conditions (C3 and C4) is greater than less constrained conditions (C1 and C2). In the non-paretic and both hands of healthy participants, CV is consistently low and similar across four conditions. Data presented are mean ± SEM. *: Significant difference between conditions in stroke participants; §Significant difference between stroke and healthy older participants; †Significant difference between stroke and all healthy participants (P's < 0.05).

when the grip dynamometer was fixed at the distal end of the arm-rest (C4). Similar MVGF magnitude between the standard (C2) and arm-rest positions (C3) suggests increased MVGF magnitude in C4 results from task differences related to external fixation of the dynamometer rather than the arm-rest alone.

Previous work has demonstrated marked differences in the neural control and muscle activation of gripping between free and fixed dynamometer conditions (Fischer et al., 2009; Kornecki et al., 2001). Compared with other conditions, C4 (fixed gripper) likely reduces task complexity by reducing the DoF and requirements for control of UE position during grip (Bernstein, 1967; Fischer et al., 2009; Kornecki et al., 2001). Consistent with our results, previous studies have reported that reduced DoF is associated with increased magnitude of maximal force production, accompanied by reduced activity in wrist stabilizing muscles (Fischer et al., 2009; Kornecki et al., 2001) and increased activity of primary movers (Kornecki et al., 2001). This finding is relevant to the design of rehabilitation interventions and devices that seek to optimize distal arm motor function post-stroke.

The next highest MVGF magnitude occurred in the least constrained, free, condition (C1), where participants used their preferred position to grip. Despite slight differences among individuals, we found participants' preferred positions were generally similar to C2 regardless of group. Perhaps surprisingly, without instruction most participants were consistently able to find the position that produces higher MVGF than C2. The ability to consistently find a preferred grip position may be associated with proprioception (Sainburg et al., 1993; Sainburg et al., 1995). Consistent with the putative importance of proprioception, one post-stroke participant studied revealed severely impaired UE proprioception on clinical examination; unlike our other participants, this individual produced 30% less MVGF in C1 than C2. Impaired proprioception is also associated with failure to control the interaction forces that arise between limb segments (Sainburg et al., 1993), which may further compromise MVGF production in such individuals.

4.2. MVGF between-trial stability is reduced in the paretic hand of individuals post-stroke

Motor output varies somewhat with repeated execution of the same task. Across trials, the variability observed is known as trial-to-trial variability (Christou and Carlton, 2002), or stability, and often quantified using the CV. We found CV of MVGF was consistently small in healthy individuals and revealed no significant differences between healthy young and older adults or between dominant and non-dominant hands. In contrast, CV was increased in the paretic hands of individuals post-stroke, independent of condition. Over the course of the experiment, no significant trend in MVGF was revealed in any hand or group, thus this reduced paretic hand stability cannot be attributed to systematic effects, most specifically fatigue. Some possible reasons contributing to reduced paretic hand stability are discussed below.

4.2.1. Voluntary muscle activation deficits

Regardless of age, neurologically intact individuals demonstrate ability to achieve close to maximal voluntary muscle activation in UE muscles (De Serres and Enoka, 1998; Klein et al., 2001; Phillips et al., 1992). After stroke, preserved ability to activate muscles has been shown in the non-paretic limb (Miller et al., 2009), although at levels slightly lower than age-matched healthy controls (Bowden et al., 2014). In the paretic limb, however, voluntary muscle activation deficits are revealed (Bowden et al., 2014; Clark et al., 2006; Li et al., 2014), especially in distal UE muscles, and are suggested to contribute to hand weakness (Hoffmann et al., 2016). In healthy adults, trial-to-trial force variability is lower at maximal (i.e., 100% MVGF) compared to submaximal effort (i.e., 80% MVGF) (Sherwood and Schmidt, 1980). Complete motor unit recruitment at maximal force levels may contribute to this phenomenon (Milner-Brown et al., 1973a, 1973b), leading to the suggestion that incomplete activation of the motor neuron pool may be associated with increased trial-to-trial force variability (Shechtman and Taylor, 2000). Although not directly measured in the current study, greater, and more frequent voluntary muscle activation deficits post-stroke can be expected to contribute to reduced paretic hand stability as observed.

4.2.2. Statistical nature of CV

Although CV has been widely used in quantifying trial-to-trial variability, it has been argued that increased CV may be driven by reduced force magnitude rather than increased variability, producing an "inflated CV" (Lechner et al., 1998; Shechtman, 2000), especially when there is an absence of proportionality between the mean and SD (Lechner et al., 1998; Portney and Watkins, 1993; Shechtman, 2000). However, we found the mean and SD of MVGF were significantly positively correlated, confirming a proportional relationship, and thus establishing validity for use of CV to quantify MVGF stability. Increased CV in the paretic hand of individuals post-stroke is more likely due to reduced stability rather than reduced MVGF magnitude.

4.3. Reduced stability in more constrained conditions in the paretic hand

Besides the overall reduction of MVGF stability, within the paretic hand of individuals post-stroke, MVGF stability varied among conditions; CV was increased with greater (i.e., C3 and C4) compared to less constrained (i.e., C1 and C2) conditions. Fig. 5 illustrates that mean paretic hand MVGF is consistent across conditions, while SD varies, ruling out the possibility of an "inflated CV" (Lechner et al., 1998; Shechtman, 2000) and further supports that increased CV in C3 and C4 results from reduced stability. Of note, CV was similar across all four conditions in the non-paretic hand and both hands of healthy adults. The source of reduced paretic hand stability remains unclear, but is of great importance for stroke rehabilitation as discussed below.

Abnormal synergies are frequently observed in the UE post-stroke (Brunnstrom, 1970; Dewald et al., 1995); these may be revealed as off-axis movements (Chae et al., 2002; Lang et al., 2005) and/or off-axis torques (Dewald and Beer, 2001; Ozawa et al., 2009;Soechting and Flanders, 2008; Ye et al., 2014) during force production. Previous studies have found increased off-axis torques during isometric single joint tasks (Dewald and Beer, 2001), reach and grasp (Ozawa et al., 2009), and grip force production (Soechting and Flanders, 2008; Ye et al., 2014) in the paretic side post-stroke. Although not measured in the current study, it is likely that off-axis UE movements and/or torques were increased during grip in the paretic hand of individuals post-stroke compared to healthy adults (Chae et al., 2002; Dewald and Beer, 2001; Lang et al., 2005; Ozawa et al., 2009; Soechting and Flanders, 2008; Ye et al., 2014). Importantly, while external constraints may have limited off-axis movements in the paretic arm and hand this technique may concurrently exacerbate off-axis torque production. Manifestations of abnormal synergies are argued to be exaggerated in the presence of external biomechanical constraints (Beer et al., 2004), which may contribute to greater off-axis torques in the paretic hand during grip with external constraints. Due to slight changes of arm and hand posture across trials (Soechting and Flanders, 2008), both the direction and magnitude of off-axis torques can vary from trial-to-trial contributing to reduced MVGF stability. In healthy adults and the non-paretic hand of individuals post-stroke, off-axis torques during grip are consistently of low magnitude (Ye et al., 2014), thus do not contribute to differences in MVGF stability across all four conditions. Similarly, when individuals post-stroke grip with the paretic hand in the absence of external constraints, off-axis torque magnitudes are likely not sufficiently great to detract from MVGF, thus explaining the consistency in less constrained conditions.

4.4. Clinical implications

The four grip conditions studied here ostensibly reflect similar biomechanics. However, MVGF magnitude and stability differed significantly among conditions, suggesting these four configurations actually represent different motor tasks. While healthy individuals have the neuromechanical resources to produce consistent MVGF regardless of biomechanical constraints, in stroke survivors MVGF stability varied across conditions. Perhaps surprisingly, conditions with fewer external constraints revealed greater stability, while conditions with more external constraint revealed less stable MVGF in stroke survivors. Conditions which exaggerate force variability are likely to compound and influence the structure and organization of movement. This information can potentially be incorporated into the design of assessments, rehabilitation interventions, and devices.

4.4.1. Assessments

Obtaining consistent and comparable measurements is an important consideration when choosing a biomechanical configuration for testing MVGF. The ASHT 'standard position' is currently the most widely used for MVGF testing in healthy adults, is relatively straightforward to instruct, and reduces the influence of variations in joint position to yield comparable MVGF values across individuals, testers, and sites (Fess, 1992). However, due to muscle weakness and production of abnormal synergies, it is often difficult for individuals post-stroke to attain the standard position and maintain it during MVGF production with the paretic hand. Predicated on the assumption that external constraints limit extraneous movements, many studies apply such measures to the paretic arm when studying grip (Ekstrand et al., 2015; Lodha et al., 2012, 2013; Martins et al., 2015a, 2015b; Persson et al., 2015; Ye et al., 2014). Rather than the intended outcome, however, the presence of external constraints alters the motor task presenting instead a novel challenge to coordination and performance. Consistent with this premise, our results illustrate that external biomechanical constraints actually impair paretic hand MVGF stability.

4.4.2. Interventions and devices

During task-specific training (i.e., practice of functional tasks), use of external constraints to prevent off-axis movements may actually exacerbate aberrant force production and reinforce inappropriate motor patterns. Based on principles of neuroplasticity, people are expected to, "gain what they have trained" (Bayona et al., 2005; Kleim and Jones, 2008). Repetitive practice of tasks using external constraints may therefore reinforce an individual's abnormal motor patterns leading to maladaptive plasticity. On the other hand, external constraints could potentially be leveraged for therapeutic benefit. Based on principles of error-based learning (Diedrichsen et al., 2010; van Dijk et al., 2005), feedback from tasks that increase motor performance variability and maximize pathological neural control strategies (i.e. greater external constraints) could be usefully incorporated into rehabilitation interventions to train stroke survivors to reduce motor output variability.

4.5. Limitations of study

Although off-axis torques during grip are likely present in the paretic hand of individuals post-stroke, their measurement was beyond the scope of this study. In combination, previous reports of off-axis torque production and current results provide rationale for measuring multi-directional torques and EMGs during grip in future work.

5. Conclusions

This is the first study to compare the magnitude and stability of MVGF across biomechanical conditions of varying external constraint. Across both healthy and stroke groups, MVGF is highest in the most constrained condition. However, external constraints alter the motor task reducing the stability of paretic hand MVGF in individuals post-stroke. Our findings have important implications for clinical assessment, especially when establishing methods to compare data across time, studies, and sites. More importantly, our results emphasize that efforts to limit the off-axis movements actually impair the stability of motor performance, particularly in the presence of neuropathology, with implications for design of rehabilitation interventions and devices.

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Ethical approval and informed consent

Approval for all procedures was attained from University of Florida Health Science Center Institutional Review Board (IRB-01) #136-2008. Informed consent was obtained from all individual participants included in the study.

Conflict of interest

The authors declare that they have no conflict of interest.

Authors' contributions

QD and CP designed the study, interpreted the results, and drafted and revised the manuscript. QD carried out the experiments and analyzed the data.

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