Research Report

Affected and unaffected quantitative aspects of grip force control in hemiparetic patients after stroke

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ABSTRACT

Adequate grip force modulation is critical to manual dexterity and often impaired in hemiparetic stroke patients. Previous studies in hemiparetic patients suggest that aspects of grip force control may be differently affected by the lesion. We developed a visuomotor power grip force-tracking task allowing quantification of tracking error, force variability and release duration. We investigated force control in 24 chronic stroke patients with varying severity of hemiparesis and in healthy control subjects. Force tracking was performed at 10, 20, and 30% maximal voluntary contraction (MVC). Control subjects were also tested at absolute force levels similar to those of the patients.

Patients tracking with their paretic hand at similar relative (%MVC) grip force levels showed increased error, force variability and release duration, but surprisingly, there was no difference in tracking error or variability between patients and control subjects performing at similar absolute force levels. Furthermore, patients improved their tracking performance across repeated blocks similar to control subjects. Release duration, however, was increased (also in the non-paretic hand), was force-independent and did not correlate with MVC strength. Of the three performance measures, only release duration explained some of the variance in arm and hand function (Frenchay Arm Test score), independent of MVC strength. The findings show (i) that hemiparetic stroke patients preserve the ability to modulate (generate and maintain) power grip force within their limited force range and (ii) that MVC grip strength and duration of grip release are differently affected and are two complementary predictors of arm function after stroke.

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Stroke, a leading cause of adult disability, often impairs manual strength, force control and dexterity causing functional limitations in activities of daily living (ADL), e.g. in grasp, in object manipulation and in tool use. Although quantification of upper limb force control has been obtained in mild to moderately affected patients, a similar assessment is lacking in severely affected patients. For example, during object grasp-and-lift using a precision grip, patients showed slowed-down force generation, excessive grip force and uncoordinated grip and load forces (Avarello et al., 1988; Hermdsörfer and Mai, 1996; Hermdsörfer et al., 2003; Nowak et al., 2007). Nonetheless, the application of precision grip paradigms is restricted to less severely affected patients. Clinically, however, it would be of advantage to assess post-stroke performance of force control over the entire range of severity. A power grip paradigm might provide a common measure, since clinical observations suggest that even the most severely affected stroke patient can generate small, whole hand grip forces (Kurillo et al., 2005; Seo et al., 2009). Thus, the first goal of this study was to apply a power grip paradigm to patients over the entire range of severity and to quantitatively investigate how patients differ from control subjects in terms of force control.

Some aspects of force control have previously been obtained in severely affected patients (Chae et al., 2002; Seo et al., 2009), such as prolonged EMG onset and offset times when initiating and terminating a maximal voluntary contraction (MVC). One recent study did investigate power grip force control in nine stroke patients and the main finding was an increased step-like pattern of force generation and release in patients compared to controls (Naik et al., 2011). This step-like pattern was more affected in patients during the grip release than the generation phase (Naik et al., 2011). Another recent study in hemiparetic patients with cerebral palsy showed intact accuracy during isometric elbow force tracking despite significant reductions in maximal force (Brendvik and Roeleveld, 2012). Together these studies suggest that aspects of grip force modulation may be differentially impaired in hemiparetic patients. Force modulation is expressed by generation, maintenance and release of force (Lang and Schieber, 2009), and therefore our second goal was to quantify and conjointly evaluate grip force-tracking error, force variability and release duration.

Clinically, upper limb weakness is the prime contributor to functional status after stroke (Ada et al., 2006; Kamper et al., 2006). In fact, maximal grip strength correlates closely with upper limb functional status (Boissy et al., 1999; Lindberg et al., 2007; Mercier and Bourbonnais, 2004) and improvements in grip strength are associated with upper limb functional recovery (Harris and Eng, 2010; Heller et al., 1987). Other measures that covary with strength will supply little additional diagnostic information. For example, inadequate grip forces (Hermdsörfer et al., 2003) and increased grip force variability (Lodha et al., 2010), often found in stroke patients, may be secondary to reduced maximal grip strength (Avarello et al., 1988; Sosnoff and Newell, 2006). Thus, the third goal of this study was to investigate whether different aspects of grip force modulation, i.e. force generation, maintenance and release, could explain some of the variance of clinically assessed upper limb function, independent of maximal strength.

We put forward the following three hypotheses:

1. Stroke patients will exhibit larger tracking error, force variability and release duration during power grip than control subjects. This is a simple extrapolation of previous studies that describe a lower ability of force control, however, measured in different tasks and less severely affected patients (e.g., Avarello et al., 1988; Chae et al., 2002; Hermdsörfer and Mai, 1996; Lodha et al., 2010; Nowak et al., 2007; Seo et al., 2009).

2. Since error and force variability have been shown to decrease with increasing force in healthy subjects (Lindberg et al., 2009; Sosnoff and Newell, 2006), we hypothesize that tracking error and force variability will be force-dependent in stroke patients as well as in control subjects.

3. In monkeys with lesioned primary motor cortex, the time taken to abruptly release grip force does not systematically increase with force level (Bury et al., 2009). Release duration should therefore remain relatively constant across force levels. We therefore hypothesize that release duration will be force-independent in stroke patients and in control subjects.

2. Results

2.1. Clinical measures of upper limb function

Severity of upper limb deficits, assessed by the FAT score, varied from mild to severe: five patients were mildly, 5 moderately and 14 severely affected (Table 1). Compared to control subjects (mean ± SD: 441 ± 124N), average maximal grip force in the paretic hand was reduced by about 75% (112 ± 72N, P < 0.001). There was also a smaller but significant (362 ± 101N, P = 0.02) reduction of 20% in the non-paretic hands compared to control subjects. No differences were found between right and left hemiparetic patients in any of the clinical measures, neither in time since stroke, nor in age (P > 0.5).

2.2. Power grip force tracking: at similar relative (%MVC) target levels in patients and control subjects

Patients were able to reach their target force as required by the task. Average rate of force increase during ramp was 88 N/s in controls, 22 N/s in the paretic hand and 72 N/s in the non-paretic hand. The difference for the paretic (75%) and non-paretic hand (18%) compared to controls is fully explained by the correspondingly lower MVC of the patients. Fig. 1 shows example trials from six patients with varying degree of paresis and from 3 control subjects. Since there was no statistical difference in any force-tracking parameter between right or left hemiparetic patients (P > 0.3), data from left and right paretic hands were pooled. In terms of performance measures, similar results were found for the ramp and hold phase. Only ramp phase data are shown below.
(i) Error: Patients produced greater error with their paretic hand than control subjects (Group effect, $F=30.5$, $P<0.001$, Fig. 2A). In contrast, on the non-paretic side, the error was not significantly different from controls (Fig. 2A). The error was force-dependent, i.e. greater error was found at low forces across control subjects, as well as across patients (Fig. 2A, $P<0.001$). Post hoc comparisons revealed significant differences in error in the paretic hand between the 10 and 30% MVC, 10 and 20% MVC and between the 20 and 30% MVC levels ($P<0.001$). Significant differences in error in the non-paretic hand were found between the 10 and 30% MVC, 10 and 20% MVC levels ($P<0.001$). No significant differences in error were found in control subjects across different force levels ($P>0.09$).

(ii) Variability: Coefficient of variation (CV) was significantly higher in the paretic hand of patients compared to control subjects (Group effect, $F=33.8$, $P<0.001$, Fig. 2B). No difference was found in the non-paretic hand. CV was highly force-dependent: the highest CV was found at the 10% force level (mean 3.0, 2.2, and 1.7 at 10, 20 and 30% respectively, Fig. 2B) both in control subjects as well as in the paretic and non-paretic hands of the patients ($P<0.001$).

(iii) Release duration: Release duration was dramatically increased and about 200 ms longer in the paretic hands than in control subjects (Group effect, $F=43.1$, $P<0.001$, Fig. 2C). Time taken to reduce the grip force in the non-paretic hand was smaller compared to the paretic hand, but still significantly larger (by about 60 ms) compared to controls (Group effect, $F=12.8$, $P<0.001$, Fig. 2C). Release duration was not force-dependent, neither in control subjects, nor in patients (Force effect, $P>0.6$, Fig. 2C).

Time since stroke and age of the patients did not correlate with maximal force, tracking error, CV or release duration ($P>0.4$).

2.3. Power grip force tracking: at identical absolute target levels in patients and control subjects

(i) Error: control subjects tracking at absolute target force levels similar to those of the stroke patients did not produce less error (Fig. 1 for qualitative illustration; group profiles shown in Fig. 2A, $P>0.5$).

(ii) Variability: CV at similar absolute force levels did not differ between stroke patients and control subjects (mean CV: controls 3.3, hemiparetic patients 3.7, Group effect $F=1.0$, $P=0.33$, Fig. 2B).

(iii) Release duration: a distinct group difference in release duration remained, even when control subjects performed at the same absolute force levels (Fig. 2C, controls mean = 106 ms, hemiparetic patients mean = 283 ms, Group effect $F=16$, $P=0.001$).

2.4. Force-tracking error and CV: a smooth function of target force

Force-tracking error was found to vary smoothly with target force level (Fig. 3). An exponentially decaying function provided a good fit to these data. At 10, 20 and 30% MVC respectively, partial linear regressions showed no differences in slope between the patient’s paretic hand and the control subjects at the same absolute force levels ($P>0.3$, Figs. 3A–D). Surprisingly, the error decreased smoothly and exponentially over the entire range tested for the paretic hand (10, 20 and 30%) as well as for the corresponding control subjects, whose data completely overlapped with those of the patients. A similar exponential error-force relation, but in a higher force range, was found for the non-paretic hand, which overlapped to a certain extent with those of the control subjects (Figs. 3A–D).

CV, which was also force-dependent (Fig. 2A), showed a qualitatively similar exponential decay as a function of force level ($CV=4.3*e^{-0.03*Force}$, not shown).

2.5. Delayed onset of grip force release does not explain prolonged release duration

Control subjects started to reduce force (onset of release) about 100 ms before the end of the hold period (mean $=133±48$ ms). In both the paretic and non-paretic hands of patients the onset of release occurred after the end of the hold period (mean $=879±622$ ms and $79±318$ ms, respectively). Group differences in release duration were tested against release onset as a covariate. Release durations were significantly prolonged for both paretic and non-paretic hands compared to control subjects independent of release onset ($F=7.9$, $P=0.008$, and $F=7.62$, $P=0.009$, respectively).

2.6. Power grip force tracking: short-term adaptation

Motor adaptation occurred for release duration and for CV (Fig. 4), but not for tracking error (force levels pooled). A decrease of release duration between the first and sixth blocks was observed in the paretic hand of 18 patients (i.e. 75%). The mean release duration decreased by 31% in the paretic hand across all patients (Fig. 4A). In the non-paretic hand, mean release duration decreased by 23% across all patients and by 16% in control subjects. The ANOVA revealed a significant Block effect ($F=6.5$, $P<0.001$) and there was no difference in learning between paretic, non-paretic or control hands ($P>0.05$).

The mean CV of the paretic hand decreased by 16% between the first and sixth blocks (Fig. 4B), and that of the non-paretic hand by 30%. Similarly, in control subjects the CV decreased by 16%. There was a significant Block effect ($F=8$, $P<0.001$) and no difference between paretic, non-paretic or control hands in terms of short-term adaptation ($P>0.05$).

2.7. Relation between grip force control and clinical measures

As could be predicted from our data on the force dependence of error and CV, we found negative correlations between MVC grip strength and error ($R=-0.76$, $P<0.001$) and CV ($R=-0.57$, $P=0.004$). Thus, the weakest patients had both the highest error and the highest CV. In contrast, there was no significant correlation between release duration and MVC grip strength ($R=-0.36$, $P=0.09$). Table 2 shows how different aspects of grip force control correlated with clinical measures of upper
Table 1 – Clinical data of the 24 hemiparetic stroke patients.

<table>
<thead>
<tr>
<th>Gender/ Age</th>
<th>Hemi side</th>
<th>Lesion type/ location</th>
<th>T since stroke (months)</th>
<th>Dom. hand</th>
<th>Proprioception (0-2)</th>
<th>Modified Ashworth Scale (0-5)</th>
<th>Grip strength (%)</th>
<th>Frenchay (0-5)</th>
<th>Barthel (0-100)</th>
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<td>S1 M 33 R</td>
<td>I/total MCA</td>
<td>110</td>
<td>R 2 3 3</td>
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<td>3</td>
<td>100</td>
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<td></td>
<td></td>
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<tr>
<td>S2 F 72 R</td>
<td>I/sup. MCA</td>
<td>96</td>
<td>R 2 2 2</td>
<td>85</td>
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<td>100</td>
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<tr>
<td>S3 M 66 R</td>
<td>H/FR/w-p</td>
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<td>R 2 3 3</td>
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<td>1</td>
<td>95</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S4 M 52 R</td>
<td>I/total MCA</td>
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<td>R 2 2 2</td>
<td>40</td>
<td>3</td>
<td>95</td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td>H/IC</td>
<td>24</td>
<td>R 1 0 0</td>
<td>45</td>
<td>5</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>I/total MCA</td>
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<td>R 1 2 2</td>
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<td>1</td>
<td>100</td>
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<tr>
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<td>H/IC, w-p</td>
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<td>L 1 4 4</td>
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<td>1</td>
<td>100</td>
<td></td>
<td></td>
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<tr>
<td>S8 F 26 R</td>
<td>H/w-p</td>
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<td>R 2 2 2</td>
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<td>1</td>
<td>45</td>
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<tr>
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<td>I/total MCA</td>
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<td>R 2 4 4</td>
<td>7</td>
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<td>80</td>
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<tr>
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<td>I/sup. MCA</td>
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<td>R 2 0 0</td>
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<td>100</td>
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<td>S12 F 72 R</td>
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<td>372</td>
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<td>1</td>
<td>95</td>
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<tr>
<td>S13 M 46 L</td>
<td>I/deep MCA</td>
<td>126</td>
<td>R 2 2 2</td>
<td>28</td>
<td>3</td>
<td>95</td>
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<tr>
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<td>R 2 1 1</td>
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<td>4</td>
<td>95</td>
<td></td>
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<tr>
<td>S15 M 56 L</td>
<td>H/IC, BG</td>
<td>87</td>
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<td>3</td>
<td>100</td>
<td></td>
<td></td>
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<tr>
<td>S16 F 46 L</td>
<td>I/total MCA</td>
<td>96</td>
<td>R 2 3 3</td>
<td>24</td>
<td>1</td>
<td>95</td>
<td></td>
<td></td>
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<tr>
<td>S17 M 54 L</td>
<td>I/total MCA</td>
<td>36</td>
<td>R 1 2 2</td>
<td>20</td>
<td>1</td>
<td>85</td>
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<tr>
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<td>I/sup. MCA</td>
<td>60</td>
<td>R 2 2 2</td>
<td>16</td>
<td>1</td>
<td>95</td>
<td></td>
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<tr>
<td>S19 F 37 L</td>
<td>H/IC, BG</td>
<td>102</td>
<td>R 1 2 2</td>
<td>22</td>
<td>0</td>
<td>95</td>
<td></td>
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<tr>
<td>S20 F 60 L</td>
<td>I/total MCA</td>
<td>36</td>
<td>R 2 2 2</td>
<td>33</td>
<td>1</td>
<td>95</td>
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<tr>
<td>S21 F 36 L</td>
<td>I/deep MCA</td>
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<td>R 0 4 4</td>
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<td>95</td>
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<td>4</td>
<td>95</td>
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<tr>
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<td>L 1 2 2</td>
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<td>90</td>
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<tr>
<td>S24 M 43 L</td>
<td>H/Temporal, IC, BG</td>
<td>64</td>
<td>R 2 4 4</td>
<td>31</td>
<td>2</td>
<td>100</td>
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Grip strength of hemiparetic hand expressed as % of non-hemiparetic hand. (T=time, Dom=dominant, I=infarction, H=haemorrhage, MCA=middle cerebral artery, sup.=superficial, BG=basal ganglia, IC=internal capsule). Proprioceptive assessment (0=absent, 1=impaired, 2=intact (Fugl-Meyer et al., 1975).
limb function. Higher FAT scores were related to greater MVC grip strength (Fig. 5A), with lower CV, and with shorter release duration (Fig. 5B). Individual characteristics of grip force control, based on MVC strength, tracking error and release time, varied among the patients. Patient profiles for the paretic hand were examined by expressing MVC strength, error and release duration as multiples of the SD of these variables in control subjects. Values >2SD indicate deficient performance, whereas values <2SD indicate performance within the normal range. Deficient MVC grip strength was found in 20 patients, deficient precision, i.e. high tracking error, in 22 patients, and deficient release duration in all 24 patients. Thus, release duration was the only variable that was impaired in all stroke patients. Even the 4 stroke patients with seemingly normal MVC grip strength had difficulty in reducing grip force abruptly. Patients with similar levels of upper limb function (similar FAT scores) had varying degrees of deficiency in MVC strength and in release duration.

Finally, a multiple regression analysis (FAT score=dependent variable; MVC strength, error, CV and release duration=independent predictors) showed that only release duration explained a significant part of the variance in the FAT score, independent of maximal grip force (semipartial correlation, $R = -0.26$, $P = 0.05$).

3. Discussion

The power grip tracking task proved feasible for quantification of the accuracy of grip force control in mildly to severely affected (including spastic) hemiparetic stroke patients. Thus, this task is suitable for severely affected stroke patients, where many other scales of upper limb function show floor effects (Miller et al., 2010). The main findings were: (i) Patients showed increased error and force variability when tracking at similar relative grip force levels (i.e. 10, 20, 30% MVC force) with their paretic hand compared to control subjects. However, there was no difference between patients and control subjects (neither in error nor in CV) when tracking at identical absolute force levels. (ii) As predicted, tracking error and variability scaled as a function of target force. This indicates that stroke patients can generate and hold low grip forces just as well as control subjects can. (iii) Release duration was prolonged in patients when tracking in relative and absolute terms and was the only parameter that explained some of the variance in clinical hand function independent of MVC grip strength. Together, these findings show that specific aspects of grip force control are affected in stroke patients, but others are not.

3.1. Non-affected aspects of grip force control

3.1.1. Stroke patients vs. controls at similar absolute force levels: intact precision

Grip force control has not been investigated previously in severely affected stroke patients. We provide for the first time quantitative evidence that, within the range given by their low MVC strength, stroke patients can generate and maintain (ramp-up and hold) power grip force in their paretic hand to a
similar degree as control subjects can. This result contradicts our first hypothesis and general qualitative clinical post-stroke observations. It also goes against earlier (Hermendörfer and Mai, 1996) and recent (Naik et al., 2011) quantitative observations of deficient grip force modulation in stroke patients. This result indicates that some aspects of force control during isometric force tracking remain intact (Brændvik and Roeleveld, 2012; Kurillo et al., 2005). In fact, when tracking at similar absolute force levels, there was no difference in error or CV between patients and control subjects, even when MVC strength was as low as 10%. A similar CV at identical absolute force levels would be expected given two assumptions: that (i) patients and controls produce similar muscle forces to achieve identical grip forces, and that (ii) CV results from signal-dependent noise. It has been shown (Jones et al., 2002) that force variability (expressed in SD) scales linearly with signal-dependent noise and is a by-product of the motor unit pool organization and not of the central motor command.

The finding of a non-affected error and CV is particularly relevant given that everyday tasks require control of absolute forces. We consider the apparent increase (as in other studies (Chae et al., 2002; Lodha et al., 2010; Seo et al., 2009)) in error and CV at comparative %MVC force levels in the hemiparetic hand as a direct consequence of the absolute force level of the tracking task. This is consistent with (i) a similar force-dependency of error and of variability in patients and in controls (in line with previous findings (Sosnoff and Newell, 2006)), (ii) data from patients and controls that fit the same exponentially decreasing function between error (or CV) and absolute force (Fig. 3), and (iii) a negative correlation between error (or CV) and MVC grip strength. Therefore, the higher CV of the patients at comparable effort (MVC) is not in contradiction with them having similar CV at identical absolute forces.

Intact tracking precision in patients can be explained by a maintained ratio between the range of force and its degree of modulation. The most parsimonious explanation for this maintained ratio is that a common neural substrate determines both parameters: would one (cortical) region provide the substrate for the first parameter, and another the substrate for the second, then stroke (typically with a large heterogeneity in terms of the affected regions) would presumably influence each parameter differently. This would then lead to changes in the ratio and consequently impair performance, but this was not the case. Multiple descending systems may underlie the ability of hemiparetic stroke patients to adequately modulate grip forces within a limited low range. However, given the importance of the corticospinal (CS) system for grip force control (Lemon, 2008; Maier et al., 2002; Nowak et al., 2007) and for post-stroke recovery of hand function (Lindberg et al., 2007; Ward et al., 2007), we consider it likely that residual CS fibres, probably via small-diameter fibres less susceptible to injury.

Fig. 2 – Tracking error (A), CV (i.e. SD/mean) (B) and release duration (C) for paretic and non-paretic hands of stroke patients and for control subjects tracking at similar relative force levels (10, 20, and 30% MVC) and similar absolute force levels (corresponding to about 2.5, 5, and 7.5% MVC) (ControlSAF=control at similar absolute force). Data are means ± 95% confidence intervals. Note that the CV (a relative measure of variability) decreases with increasing force (B), while the SD (an absolute measure of variation) increases with force (not shown).
Blight, 1991), allow for adequate force modulation post-stroke. However, we cannot exclude the interplay of other structures, directly or indirectly affected by stroke, such as the reticulospinal (Riddle et al., 2009) or propriospinal (Alstermark et al., 2007) system.

3.1.2. Intact motor adaptation in stroke patients

Patients showed similar short-term adaptation in terms of reduced variability and shortened release duration across repeated blocks of visuomotor tracking as did control subjects. This suggests an intact capacity for force control adaptation in stroke patients, which likely involves multiple cortical regions, basal ganglia and cerebellum (Tomassini et al., 2011).

3.2. Affected aspects of grip force control

In addition to MVC strength, release duration was affected in both the paretic and non-paretic hands. Release duration was almost three times longer in the paretic hand compared to controls, even when accounting for prolonged release onset, which speaks against a generalised slowing of motor actions post-stroke (Godefroy et al., 2010). Our finding is coherent with hemiparetic patients showing longer electromyography termination times (Chae et al., 2002; Seo et al., 2009) and difficulty in letting-go of grasped objects (Beebe and Lang, 2009).

Importantly, our study shows that release duration is not dependent on target force level, i.e. does not scale with force, nor is

Fig. 3 – Relation between ramp error and absolute force. Symbols indicate group and condition: grey square: patients, paretic hand; open square: patients, non-paretic hand; black circle: controls; open circle: controls at same absolute force (SAF) level. Ramp error vs. absolute force corresponding to 10% MVC (A), to 20% MVC (B) and to 30% MVC (C). D. Ramp error vs. absolute force corresponding to the entire range tested for all 4 groups. The error-force relation can be expressed by an exponential decay (regression line: Error = 95e^(-6.7*Force)).
it correlated with MVC grip strength. Thus grip force release is not simply the mirror image of force generation. This agrees with findings from behavioural, lesion and imaging studies (Bury et al., 2009; Chae et al., 2002; Spraker et al., 2009). It is debatable whether the neural substrate of force release resides within the CS system (Buccolieri et al., 2004; Pope et al., 2007) and operates through activation of inhibitory spinal interneurons (Maier et al., 1998) or whether additional systems come into play, such as cortico-striatal loops (Toxopeus et al., 2007) or modulatory brain stem systems (Seo et al., 2011). There is evidence for impaired inhibitory mechanisms after stroke at cortical (Hummel et al., 2009) and spinal levels (Lamy et al., 2009). However, our data do not permit a more precise pinpointing.

3.3. Clinical implications

3.3.1. Left vs. right hemiparesis and affected vs. non-affected hand

A number of findings from this study are of clinical relevance. First, we did not find any difference in error, CV or release duration between patients with right or left hemiparesis. This is largely in line with other studies on post-stroke force control (Noskin et al., 2008; Nowak et al., 2007; Sunderland et al., 1999), but differs from findings on ipsilesional arm kinematics (Hermsdörfer et al., 2003; Robertson et al., 2009). A possible explanation for these differences is that power grip represents a more lateralized task mainly involving contralateral cortical areas (Ehrsson et al., 2000), whereas reaching involves a more bilateral network (Tanji et al., 1988). This finding suggests that a similar approach to rehabilitation of grip function can be used for left and right hemiparetic patients.

Second, the non-paretic hand was also affected: maximal grip strength was decreased by approximately 20%, comparable to previous findings (Colebatch and Gandevia, 1989). However, in the non-paretic hand error and CV did not differ significantly from that in controls, whereas release duration did. Prolonged release duration in the non-paretic hand has been reported previously (Seo et al., 2009). Therefore, grip force release (re)training may help restore dexterity to the non-paretic hand after stroke (Noskin et al., 2008).

3.3.2. Covariation vs. independence of performance measures with grip strength

We found a clinically relevant covariation of performance measures with grip strength. Maximal grip strength explained 59% of the variability in the patients’ FAT scores, comparable to previous reports (Boissy et al., 1999; Mercier and Bourbonnais, 2004). In addition, grip force-tracking error explained 44%, CV 24% and release duration 29% of the variance in FAT scores (univariate analyses). Maximal grip strength also showed the strongest correlations with clinically rated spasticity, consistent with the fact that maximal grip force is a good predictor of overall upper limb function after stroke (Ada et al., 2006; Boissy et al., 1999; Kamper et al., 2006; Mercier and Bourbonnais, 2004).

More importantly, release duration was the only parameter that explained some (7%, multivariate analysis) of the variance of FAT scores independent of maximal grip force, and although not routinely assessed, it could be clinically useful: it was the only parameter showing (i) a significant difference in the non-paretic hands in patients, (ii) a significant improvement over...
subsequent trials in most patients, and (iii) a deviation beyond 2SD of controls in each patient. This suggests that release duration has a good sensitivity (i.e. detects subtle ipsilesional deficits, monitors short-term changes, provides a marker for most stroke patients) and is a clinically relevant measure, complementary to maximal strength.

3.4. Methodological limitations

First, the cohort of stroke patients in this study was heterogeneous, in terms of lesion types and locations, as well as in terms of upper limb impairment. Variability of lesion extent may limit generalisation of our results, however, it is all the more remarkable that a simple, unique relation was found between force level and tracking error. Future neuroimaging studies will help clarify if grip force control parameters, as quantified in this study, are contingent upon lesion location and how they depend on residual neural structures. The degree of upper limb impairment also varied widely in the cohort (from mild to severe), but this was on purpose and allowed us to establish correlations between grip force control parameters and upper limb function. Second, a power grip paradigm, though advantageous in terms of feasibility, cannot capture behavioural parameters of manual dexterity previously shown to be impaired after stroke, such as directional components in precision grip (Seo et al., 2010) or independence of finger movements (Schieber et al., 2009).

3.5. Conclusions

The visuomotor power grip force-tracking task was suitable for quantification of force control in stroke patients, even in severely hemiparetic patients. This study, the first to compare similar absolute levels of force control in stroke patients and controls, surprisingly showed that precision and adaptation of grip force tracking remain intact within the limited force range of the paretic hand. In contrast, release duration was prolonged in both the paretic and non-paretic hands and was the only parameter explaining some of the variance of hand function independent of maximal grip strength, suggesting release duration to be a clinically useful measure.

4. Experimental procedures

4.1. Participants

A total of 24 chronic hemiparetic stroke patients were recruited (age=26–72, mean=48 years; 11 women, 13 men; 24–372 months post-stroke, median=72 months). Twelve patients had right and 12 had left hemiparesis. Inclusion criteria: (i) ischemic or hemorrhagic supratentorial stroke, (ii) ability to communicate and understand information related to the study. Exclusion criteria: (i) previous history of neurological disorders, (ii) cerebellar lesion, (iii) clinical signs of apraxia, hemianopsia or hemineglect, (iv) upper limb botulinum toxin injection within 3 months, (v) any other disorder that may impair grip function (e.g. arthritis) or task performance.

Fifteen right-handed healthy subjects (age=28–72, mean=40 years; 7 women, 8 men), without any history of neurological disorder, constituted a first control group. The study received IRB approval from our institution, and all subjects provided informed consent according to the Declaration of Helsinki.

4.2. Clinical measures

Clinical assessments included: (i) proprioceptive function of the wrist (0=absent, 1=impaired, 2=intact (Fugl-Meyr et al., 1975)), (ii) muscle tone in finger and wrist flexors according to modified Ashworth scale, (iii) maximal voluntary grip strength (MVC) using the Jamar hand dynamometer, (iv) Frenchay Arm Test (FAT) (Heller et al., 1987) score to assess upper limb motor function (indicative of the International Classification of Functioning (ICF) activity domain), and (v) the Barthel index for assessment of independence in ADL. None of the patients had clinical signs of a grasp reflex. Severity of upper limb function was categorized according to FAT scores as mild (4–5), moderate (2–3) or severe (0–1). An FAT score of zero reflects the inability to stabilize a ruler with the paretic hand while drawing a line with the non-paretic hand (Heller et al., 1987).
4.3. Power grip force-tracking task

Subjects exerted isometric force on a power grip manipulandum consisting of two levers acting on a force transducer (resembling a nut-cracker). The manipulandum was positioned in the palm of the hand in order to measure force generated in intrinsic and extrinsic hand muscles. Subjects rested the manipulandum on their thigh and were able to maintain it for the entire duration of the task without difficulty. Output of the calibrated force transducer (range: 0–1000 N, sensitivity: 0.1 N, wwwassistmovcom) was amplified and then sampled at 1 kHz by a CED Micro1401 running Spike2 (Cambridge Electronic Design®). Grip force was displayed in real-time on a computer screen. Subjects were instructed to follow target force trajectories with the cursor as precisely as possible. The task comprised 6 blocks, each consisting of 4 ramp-hold-and-release target force trajectories (a paradigm previously used (Lindberg et al., 2010)) from 0 N to either 10, 20, or 30% MVC. Tracking at three different force levels allowed the study of systematic variations of motor control parameters as a function of force (Lindberg et al., 2009). The force generation period (ramp phase) lasted 2 s, the hold phase 4 s, and the release was instantaneous. Thus, the rate of force increase (dF/dt) during the ramp was proportional to the target force, i.e., 5, 10, or 15% MVC/s. Each subject performed a pseudo-randomised order of six blocks at each force level (i.e. 24 trials/per force level, a total of 72 trials in about 12 min). Subjects were instructed to minimize the error between the applied target force and to let-go as quickly as possible at the end of the hold period. All subjects performed the task with each hand separately, the starting hand being randomised.

The following three performance measures were quantified trial-by-trial:

1. Relative error (N.s), which reflects the total error (positive + negative) normalized to the target force level.
2. The coefficient of variation (CV) of force was used as a measure of variability (i.e., SD/mean). The CV expresses variability relative to the mean force level and is often used for the study of force variability (e.g., Enoka et al., 2003).
3. Release duration: the time taken to abruptly reduce the grip force (from 75 to 25% of the target force) at the end of the hold period. The release onset, i.e. time of initial force reduction, was also quantified as the time when the slope (dF/dt) first crossed a negative threshold (Lindberg et al., 2009).

Since stroke patients had lower maximal grip force values compared to control subjects, their absolute target force levels were consistently lower. We therefore compared their performance to a second group of 12 healthy control subjects (mean age=42 years) who used the same absolute target force levels. Each control subject performed the task with the same absolute target levels as a stroke patient with right hemiparesis.

4.4. Statistical analysis

Force data was down-sampled to 100 Hz and analyzed using Matlab v6 (The MathWorks, Inc.). Some patients had difficulty relaxing completely during baseline. Trials with an average baseline (from 1.5 to 0.5 s prior to the ramp) force exceeding 20% of target force level were considered non-valid and excluded from analysis. Nineteen patients had some non-valid trials (range 1–12). Release time was measured up to 1500 ms after the hold phase. One patient (S17) did not manage to release force consistently within this window (i.e. excluded data). Error, CV and release duration values were averaged, respectively, across the 4 trials in each block. Data was analyzed with Statistica 9 (StatSoft, Inc.). A repeated measures ANOVA was used to analyse the effects of force, block and group differences, i.e. two within subject factors: FORCE level (10, 20, and 30% MVC) and BLOCK level (6 blocks of trials) and one categorical predictor: GROUP (stroke or control). Differences between stroke groups (right or left hemiparesis) and controls (corresponding right or left hand) were tested separately.

Univariate relations between grip force control variables and clinical measures were examined using Spearman rank order correlations. A multiple regression analysis using semipartial correlation statistics was performed to examine whether the grip force variables could explain some of the variance in upper limb function (FAT score) independent of MVC grip strength. Error, CV, release duration and MVC strength were used as continuous predictors of FAT scores. The level of significance was set to P≤0.05.

Disclosures
None.

Author contributions

P.G.L. designed the study, performed the experiments, analyzed the results and drafted the manuscript. N.R. collected clinical data and interpreted the results. J.R. assessed clinical measures and edited clinical parts. A.R.B. interpreted the results and conceived of additional experiments. B.B. designed the study and interpreted the results. M.A.M. coordinated the study and edited the manuscript. All authors approved the final version for publication.

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