"Precision grip in chronic stroke patients : evaluation and rehabilitation"

Dispa, Delphine

Abstract

This thesis aims to advance the evaluation and rehabilitation of precision grip in chronic stroke patients. Stroke is a leading cause of permanent deficits worldwide, and fine manipulation skills are often disturbed in the paretic hand. The evaluation of predictive and reactive control in this population highlighted deficits in the paretic hand under both conditions. Patients also displayed a significant decrease in digital dexterity and an increase in the time taken to lift the manipulandum with the paretic hand compared with the non-paretic hand and control subjects. A specific rhythmic bilateral grip-lift task oriented therapy undertaken three times per week for 8 weeks did not modify grip-lift task parameters, digital dexterity, manual ability or subjects' satisfaction with their participation in activities of daily living. Patients' perceptions of increased ease and fluency of manipulation after therapy was not measured through these evaluations. The suggestion of changes in...

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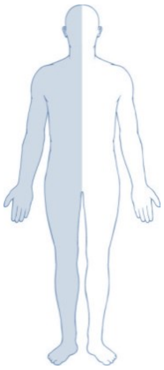
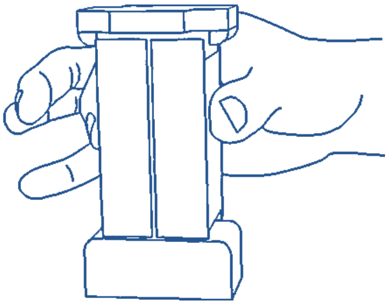
Institute of Neuroscience

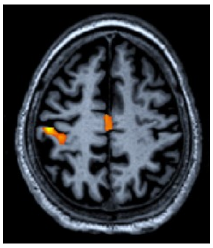
Precision grip in chronic stroke patients:

Evaluation and rehabilitation

Delphine Dispa







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"Science is a way of thinking much more than it is a body of knowledge."
Carl Sagan

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LIST OF ABBREVIATIONS

AC	anterior commissure
ADL	activities of daily living
ANOVA	analysis of variance
APA	anticipatory postural adjustments
ARAT	action research arm test
BA	Brodmann area
BATRAC	bilateral arm training with rhythmic auditory cueing
BOLD	blood-oxygen-level dependent
CIMT	constraint induced movement therapy
CF	coefficient of friction
CMA	cingulate motor area
dGF/dt	first derivative of GF with respect to time
dLF/dt	first derivative of LF with respect to time
EMG	electromyography
EPI	echo planar imaging
FDI	first dorsal interosseous
fMRI	functional Magnetic Resonance Imaging
GF	grip force
GFmax	maximum grip force
GLM	general linear model
HCP	hemiplegic cerebral palsy
ICF	International classification of functioning, disability and health

2IPS	intraparietal posterior sulcus
LF	load force
LFmax	maximum load force
LB	Lying blindfolded position
LO	Lying with open eyes position
M1	primary motor area
MAS	motor assessment scale
MEP	motor evoked potential
MMSE	mini mental state examination
MR	magnetic resonance
MRI	magnetic resonance imaging
ND	non-dominant hand
NP	non-paretic hand
P	paretic hand
PC	posterior commissure
PM	premotor cortex
PMd	dorsal premotor cortex
PMV	ventral premotor cortex
PO	parietal operculum
QOL	quality of life
RM ANOVA	repeated measures analysis of variance
S1	primary sensorimotor area
S2	secondary somatosensory area
SB	sitting blindfolded position
SD	standard deviation

SIAS	stroke impairment assessment scale
SMA	supplementary motor area
SMD	standardized mean difference
SO	sitting with open eyes position
TE	echo time
TFE	turbo field echo
TMS	transcranial magnetic stimulations
TR	repetition time
WMFT	Wolf motor function test
2D	two dimensional
3D	three dimensional
3T	three tesla

CHAPTER I: General introduction and background

Stroke is a leading cause of permanent impairment worldwide. A lesion in one hemisphere may lead to various impairments in the contralateral hemi-body. The, often incomplete, recovery displays a nonlinear, logarithmic pattern (i.e. early after stroke onset, the largest improvements are observed and gradually level off) and is related to a complex process that is observed mostly over the 3 to 6 first months after stroke (Figure I.1) (Kwakkel et al., 2006; Langhorne et al., 2011). The improvements probably occur through a combination of spontaneous and learning-dependent processes including: restitution, substitution, and compensation (Kwakkel et al., 2004b, Langhorne et al., 2011).

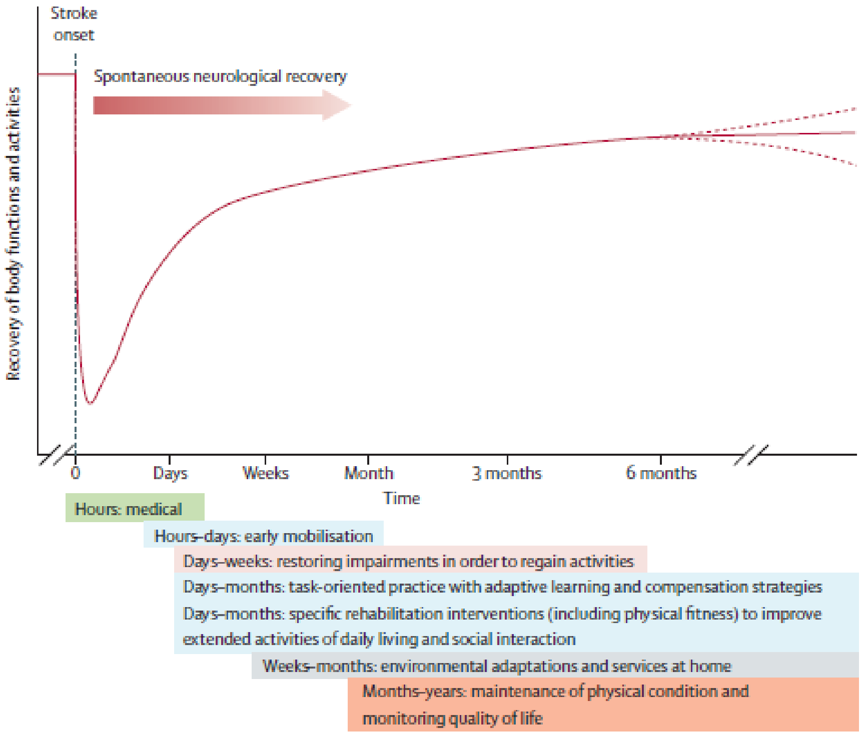

Figure I.1. Hypothetical pattern of recovery after stroke with timing of intervention strategies (Langhorne et al., 2011).

In the first to third months, a variable spontaneous neurological recovery could be a confounder of rehabilitation intervention. Indeed, Kwakkel et al. (2006) observed that progress of time (given variability in intervention modality, intensity, duration and environment) reflects spontaneous recovery of body function and activities in the first 6 to 10 weeks after stroke onset. This suggests that the progresses in functional outcome appearing after 3 months are dependent on learning adaptation strategies to acquire for example gait and activities of daily living (ADL) (Kwakkel et al., 2004b). Those results were confirmed recently with a 3-dimensional kinematic study observing smoothness improvements of hand transport and grasp aperture of the paretic upper-limb in the first 8 weeks after a first-ever unilateral stroke (van Kordelaar et al., 2014).

Functional imaging of stroke recovery displays also a temporal pattern of activation shifts. Shortly after stroke, an initial contralesional shift of activation to the “unaffected” hemisphere is observed. Then, learning-related structures activates (including the cerebellum, basal ganglia and frontal cortices). Finally, two patterns are described depending on the degree of recovery (depending itself on the amount of remaining fibers in the impaired corticospinal tract), either a perilesional (refocusing), or a distributed recruitment pattern (Feydy et al., 2002; Ween, 2008). Rehme et al. (2012) confirmed this last assumption concluding that a good functional outcome relies on recruitment of the original functional network rather than contralesional activity. Richards et al. (2008) demonstrates an increased activity within the lesioned hemisphere after an upper extremity rehabilitation program. Even though, the mechanisms by which therapy enables functional recovery remains unclear (Eliassen et al., 2008).

Rehabilitative physical therapy treatment favoring intensive high repetitive task-oriented and task-specific training in all phases post stroke has proved to be essential in reducing motor impairments (Veerbeek et al., 2014).

In the chronic phase after stroke, due to variable deficits in sensitivity, muscle force and manual and digital dexterity, the ability to take an object between the thumb and the index finger can be disturbed. Dextrous manipulation is essential for many routine ADL.

For these reasons, the upper limb of chronic stroke patients needs to be evaluated precisely and rehabilitation undertaken. Following the model of the

International Classification of Functioning, Disability and Health (ICF), subjects may be categorized according to body structures and functions, activity and participation. Upper limb structure and function can be assessed with various tools. In particular, digital dexterity and the coordination of the forces exerted on an object during manipulation should be assessed. Analysis of the coordination of forces during a grip-lift task permits objective quantification of manual deficits in stroke patients (Nowak, 2006). There is a clear necessity for objective evaluation; some stroke patients display a mismatch between objective outcomes and their subjective perception of upper limb function (van Delden et al., 2013a). Despite this, self-reported outcome measures may provide information that is not covered by capacity evaluation of the upper limb and vice versa.

I.1. The grip-lift task

Grip-lift task registration and analysis appears to be a sensitive method to quantify manipulative hand function (Nowak and Hermsdorfer, 2005, 2006). This method is widely used to understand and describe fine motor control in healthy subjects as well as in patients with peripheral or central nervous system problems. The adaptation of the grip-lift to environmental variations (e.g. microgravity, sudden loading) or transitory perturbations (e.g. cutaneous anaesthesia, darkness, fingertip moisture, concomitant cognitive task) can also be described through this task (Augurelle et al., 2003; André et al., 2010; Crevecoeur et al., 2011; Dispa et al., submitted; Eliasson et al., 2005; Guillery et al., 2013; White et al., 2005; White et al., 2011).

Two forces are required during the grip-lift task (Figure I.2). A vertical force called load force (LF) is recorded parallel to the contact surfaces. This force varies with the weight of the object and the vertical acceleration. The grip force (GF), perpendicular to the contact surfaces, adapts to variations in LF and the friction between the fingers and the object, and has a safety margin dependent on the subject himself (Johansson and Westling 1984). Under static conditions, the safety margin can be described as a slight increase of GF compared with the minimum needed to prevent slipping of the object. When the subject lifts the object, the vertical acceleration involves modifications of LF. GF has to fit the LF changes to maintain the safety margin, and the two forces vary synchronously (Witney et al., 2004).

GF and LF are closely synchronised while lifting and manipulating an object. The so-called cross-correlation coefficient is the maximal correlation found between the first derivatives of GF and LF (i.e. GFrate, dGF/dt; LFrate, dLF/dt; Figure I.2.C) as functions of the associated time-shift that fits both curves (Figure I.2.D) (Duque et al., 2003). In healthy adults, the scaling of the forces appears to be modified by cutaneous anaesthesia. However, the close correlation of the two forces as well as the small time-shift seems to be preserved (Augurelle et al., 2003; Witney et al., 2004).

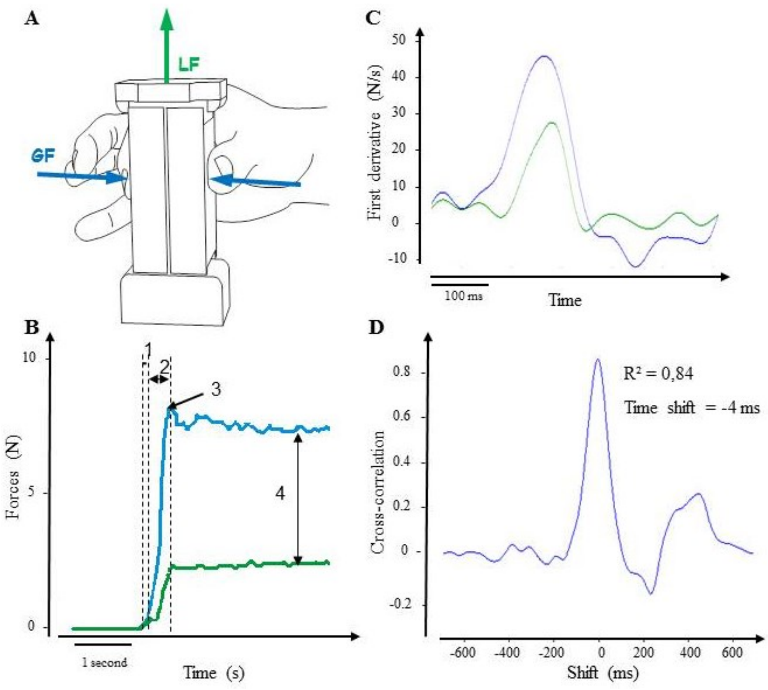

Figure I.2. Grip-lift task and forces recordings during a typical grip-lift task with the non-paretic hand of a chronic stroke subject. (A) Manupilandum taken between the thumb and index finger, blue arrows illustrates the grip force (GF); in green, the load force (LF). (B) GF (in blue) and LF (in green) as functions of time during one lift; (1) preloading phase, (2) loading phase, (3) maximum of GF (GFmax), (4) hold ratio during the stable phase (GF/LF). (C) First derivative of GF (GFrate; dGF/dt, in blue) and LF (LFrate; dLF/dt, in green) as functions of time. (D) Cross-correlation of GFrate and LFrate as functions of time shift.

Furthermore, GF is anticipatorily (feedforward model) and reactively (feedback) adjusted to LF modifications. The feedforward model is acquired through learning and experience. This permits anticipation of the forces to be applied to the object when, for example, the movement of the object involves acceleration and LF modifications to which GF must be adjusted. To adjust to the environment and to sudden modifications, the sensory system gives feedback information, thereby increasing the adaptation (Witney et al., 2004).

Grip-lift parameters can be altered post-stroke (Blennerhassett et al., 2006; Dispa et al., 2014). In stroke subjects, some grip-lift variables are modified as described by McDonnell et al. (2006). In that study, the paretic hand of subacute stroke patients showed a greater vertical negative force before lifting the object, a longer delay between the contact with the object and the beginning of the vertical force (preloading phase) and less synergy between GF and LF (a smaller cross-correlation coefficient), with respect to the non-paretic hand. The preloading phase, the maximal rate of GF and the cross-correlation coefficient were significantly correlated with the results obtained on a functional assessment scale (Action Research Arm Test - ARAT) (Hsieh et al., 1998). Hermsdörfer et al. (2003) also demonstrated a significant correlation between kinetic grasp parameters and grip strength. In clinical practice, upper extremity function is often measured through grip strength, but the precise synergy between GF and LF seems to be an important parameter in assessing the integrity of motor control.

Modifications of grip-lift parameters under reactive and predictive conditions in stroke patients are described and discussed in Chapter II.

I.2. Upper limb rehabilitation in chronic stroke patients

There appears to be a strong need for efficacious rehabilitation methods for the upper limb after stroke. Up to 20% of stroke patients display low functional activity of the arm at 6 months (French et al., 2010). A recent Cochrane review focussing on the recovery of function and mobility in stroke patients reported the potential benefit of therapy, compared with no treatment and dependent on the time since stroke (significant benefits are associated with a shorter time since stroke), on functional recovery and motor function (Pollock et al., 2014). The dose of intervention analysis presents significant benefits after 30 to 60 minutes of treatment for 5 to 7 days/week. By contrast, there was no effect concerning independence in ADL. However, the authors concluded that the substantial heterogeneity of the patients and treatments limited the evidence relating to the dose of physical therapy. Although it appears to be difficult to rehabilitate hand function, various therapies have shown good results for proximal upper limb recovery in chronic stroke patients (Nowak and Hermsdorfer, 2009).

One such rehabilitation technique is Constraint-Induced Movement Therapy (CIMT). Various modified versions of this approach have been published (McIntyre et al., 2012; Page et al., 2013). The principle of this approach is to constrain the non-affected arm and/or hand to avoid the learned non-use phenomenon and to optimise use of the affected arm. The inclusion criteria are very selective. Patients with severe impairments are not appropriate for this technique; indeed, constraint of the less affected arm could be dangerous in those with balance problems and can be deceiving through hampering ADL.

In addition to unilateral therapies, bilateral techniques have been developed. The most difficult ADL are bimanual activities (Penta et al., 2001) and these are obviously not addressed by unilateral therapies. Some authors have reported superior effects of bilateral training on bimanual activities, compared with unilateral training (McCombe Waller and Whitall, 2008). Bilateral rehabilitation can help in the treatment of post-stroke subjects with various degrees of impairment from minimal to severe. Other authors have reported the effect on cortical activation of bilateral arm training with rhythmic auditory cueing (BATRAC) (Luft et al., 2004a; Whitall et al., 2000). In this therapy, patients had to pull and push bilaterally, in synchrony or alternating, two handles sliding in the transverse plane (four 5 minute movement periods interspersed with 10 minute rest periods, three times/week) (Figure I.3). A 6 week training period seemed to lead to increased hemispheric activation (bilaterally but mainly in contralesional precentral gyrus and cerebellum) during paretic arm movements in two-thirds of the studied patients. Patients in whom cortical activation was present also displayed an increase in arm function (on Fugl-Meyer score). These results suggest that repetitive bilateral training could be a potential therapy for upper limb rehabilitation in hemiparetic stroke patients (Luft et al., 2004a).

Figure I.3. Commercial version of BATRAC, called Tailwind, produced by Encore Path, Inc. Baltimore, MD, USA and Anatomical Concepts UK Ltd, Clydeland, UK (http://www.tailmindtherapy.com) (van Delden et al., 2012a).

van Delden et al. (2013b), in a review comparing unilateral and bilateral upper limb training, concluded that, within 1 to 6 months post-stroke, modified CIMT as well as modified BATRAC seem not to be more effective then dose-matched conventional therapy in improving upper limb motor function. However, in moderately impaired chronic stroke patients, bilateral and unilateral therapies seem efficacious, with a greater impact of bilateral training on the proximal upper limb (Stoykov et al., 2009).

In another review, a unilateral versus bilateral training comparison reported different but disparate results in chronic stroke patients (van Delden et al., 2012b). Considering the ARAT and the functional ability scale of the Wolf Motor Function Test (WMFT) a significant standardized mean difference (SMD) was observed in mild upper-limb paresis patients (including post-acute and chronic subjects) in favour of unilateral treatment (Figure I.4). When chronic stroke participants were evaluated through the Motor Assessment Scale (MAS) the pooled results seem to be in favour of bilateral therapies but the small number of studies yielded to a non-significant mean difference (Figure I.5).

	Unilateral			Bilateral				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
1. Severe								
Morris 2008	10.7	19.8	12	8.4	19.5	23	8.6%	0.11 [-0.58, 0.81]
Subtotal (95% CI)			**12**			**23**	**8.6%**	**0.11 [-0.58, 0.81]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.32 (P = 0.75)								
2. Moderate								
Hayner 2010	0.18	0.56	3	0.33	0.24	3	1.6%	-0.28 [-1.90, 1.34]
Morris 2008	20.1	19.8	22	20.4	19.5	17	10.5%	-0.01 [-0.65, 0.62]
Whitall 2011	0.1	0.74	50	0	0.59	42	24.8%%	0.15 [-0.26, 0.56]
Subtotal (95% CI)			**75**			**62**	**36.9%**	**0.08 [-0.25, 0.42]**
Heterogeneity: Chi² = 0.38, df = 2 (P = 0.83); I² = 0%								
Test for overall effect: Z = 0.48 (P = 0.63)								
3. Mild								
Hayner 2010	0.56	1.01	3	0.53	1.08	3	1.6%	0.02 [-1.58, 1.62]
Morris 2008	13.5	19.8	12	13.4	19.5	11	6.3%	0.00 [-0.81, 0.82]
Suputtitada 2004	10.08	13.2	33	1.84	21	36	18.3%	0.46 [-0.02, 0.80]
Van der Lee 1999	5.8	13.1	31	1.7	13.9	31	16.7%	0.30 [-0.20, 0.80]
Wu 2011	0.52	0.71	21	0.33	0.83	22	11.6%	0.24 [-0.36, 0.84]
Subtotal (95% CI)			**100**			**103**	**54.5%**	**0.30 [0.02, 0.58]**
Heterogeneity: Chi² = 1.08, df = 4 (P = 0.90); I² = 0%								
Test for overall effect: Z = 2.11 (P = 0.03)								
Total (95% CI)			**187**			**188**	**100.0%**	**0.20 [-0.00, 0.41]**
Heterogeneity: Chi² = 2.47, df = 8 (P = 0.96); I² = 0%								
Test for overall effect: Z = 1.95 (P = 0.05)								
Test for subgroup differences: Chi² = 1.01, df = 2 (P = 0.60), I² = 0%								

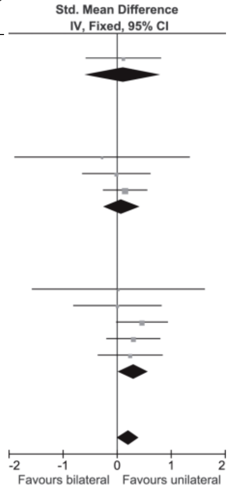

Figure I.4. Forrest Plot of the pooled Action Research Arm Test and Wolf Motor Function Test scores resulting of unilateral or bilateral therapy for severe, moderate and mild paresis subgroups. SD: standard deviation; std: standardized; CI: confidence interval; df: degrees of freedom (van Delden et al., 2012b).

	Unilateral			Bilateral				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
1. Severe								
Summers 2007	0	0	1	1	0	1		Not estimable
Subtotal (95% CI)			**1**			**1**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2. Moderate								
Stoykov 2009	0.42	1.08	12	1.14	1.4	12	100.0%	-0.72 [-1.72, 0.28]
Summers 2007	0	0	1	0.43	0.5	3		Not estimable
Subtotal (95% CI)			**13**			**15**	**100.0%**	**-0.72 [-1.72, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.41 (P = 0.16)								
3. Mild								
Summers 2007	-0.08	0.82	4	0.5	0	2		Not estimable
Subtotal (95% CI)			**4**			**2**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Total (95% CI)			**18**			**18**	**100.0%**	**-0.72 [-1.72, 0.28]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.41 (P = 0.16)								
Test for subgroup differences: Not applicable								

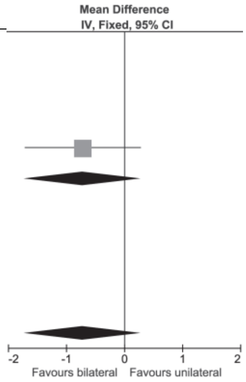

Figure I.5. Forrest Plot of the pooled Motor Assessment Scale scores resulting of unilateral or bilateral therapy for severe, moderate and mild paresis subgroups. SD: standard deviation; CI: confidence interval (van Delden et al., 2012b).

Summers et al. (2007) presented improvements in the upper limb items of the MAS in patients who underwent bilateral training for 1 week. No effect was observed in the unilateral training group. The authors suggested that normalization of intrahemispheric and interhemispheric inhibition had occurred. Indeed, the excitability of the unaffected hemisphere decreased during transcranial magnetic stimulation (TMS). Interhemispheric inhibition via the transcallosal sensorimotor fibre tract is likely to be increased in the affected hemisphere after cortical damage due to stroke (Murase et al., 2004). This phenomenon leads to further impairment of the paretic upper limb. Additionally, in the affected hemisphere itself, the location of the lesion seems to influence the pattern of the motor cortex excitability (Liepert et al., 2005). Mudie and Mathias (2000) suggested, after observing improvements related to bilateral upper limb training, that simultaneous bilateral movement promotes interhemispheric disinhibition, allowing the undamaged hemisphere to share the normal movement command. In another study, Wu et al. (2011) concluded, after 3 weeks of treatment, that bilateral arm therapy improved force generation. By contrast, modified CIMT was reported to be more appropriate for increasing functional ability and the use of the affected arm for ADL.

Finally, the quality of life (QOL) of stroke patients seem to be increased by upper limb therapies including CIMT and exercise/training programs (Pulman and Buckley, 2013). Given the small numbers of studies considering QOL as an outcome measure, these results should be confirmed through larger studies.

Some authors have described the interest to combine unilateral and bilateral therapies (Harris and Eng, 2006). The potential effect of this combination to rehabilitate grip-lift task in chronic stroke subjects, through specific grip-lift task oriented rehabilitation, is described and illustrated in Chapter III.

I.3. Brain activity in precision grip

Some therapies emphasise cortical reorganisation after stroke. As already mentioned, Luft et al. (2004a) reported the effect of bilateral training in chronic stroke patients. The contralesional hemisphere is involved in improvement of upper limb motor function. After an injury, the control of movement, especially in complex tasks, is controlled more by the contralesional hemisphere (Stoykov and Corcos, 2009).

In healthy subjects, the coordination of grip-lift forces has been described for the cerebellum using functional magnetic resonance imaging (fMRI) (Kawato et al., 2003). Comparison of brain activity during repetitive power and precision grip shows no differences when light forces are applied. However, power grip led to increased activity in the contralateral sensorimotor area (M1/S1) and ipsilateral cerebellum compared with precision grip (Kuhtz-Buschbeck et al., 2008; Ehrsson et al., 2000; Keisker et al., 2009). The reason for this increased activation remains unclear. It seems to depend on the feedback provided to the subject and the type of action realized (Kuhtz-Buschbeck et al., 2008; Ehrsson et al., 2001). In healthy adults, a precision grip with light force may be insufficiently challenging to evoke the cortical activity representative of dextrous manipulations (Kuhtz-Buschbeck et al., 2008).

The grip-load force task presented activations in ipsilateral intraparietal cortex and bilateral supramarginal cortex, the contralateral ventral premotor cortex (PMV/area 44), the supplementary motor area (SMA), the cingulate sulcus (cingulate motor area-CMA) and the central sulcus (M1/S1) cortex (Ehrsson et al., 2000; Ehrsson et al., 2001; Ehrsson et al., 2003; Kuhtz-Buschebeck et al., 2001) (Figure I.6).

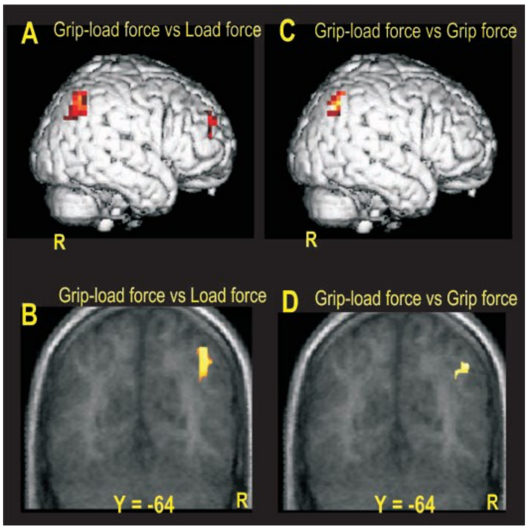

Figure I.6. From Ehrsson et al., 2003. Posterior parietal activation associated with the coordination of grip and load forces. Significant activation superimposed on 3D reconstructions (A and C) or a coronal slice (B and D) of the standard brain. A and B: Significant contrast signals in a posterior section of the right intraparietal cortex when the subjects performed a grip-load force task compared with a load force task. C and D: Activation of the same intraparietal area when the subjects performed a grip-load force task compared with a grip task. Activation maps were thresholded at each voxel at $Z > 3.09$; only significant activations ($P < 0.05$) after a correction for multiple comparisons are shown. The Talaraich coordinate is indicated for the coronal slice (B and D). L, left; R, right.

In a study describing the specific cortical activations in grip-load tasks, Ehrsson et al. (2003) compared a grip-lift task with either a grip task or a load task (Figure I.6). The conjunction analysis showed that grip-load force coupling appeared to be localized in the right intraparietal posterior sulcus (IPS).

Focussing on digit movements, non-synergistic coordination patterns displaying stronger cortical activity could be observed (Ehrsson et al., 2002). In this study, starting with an open hand with the fingers extended and subsequently flexed, fingers with the thumb extended in the “auto-stopper position” displayed greater cortical activity than opening and flexing the fingers.

When observing bimanual coordination in healthy adults, the principal brain areas involved are described in the cerebellum, SMA and CMA, premotor cortex (PM) and corpus callosum. The part of the cerebellum activated seems to be related to the synchrony of the task and the high coordination effort demand of the movement. The SMA activation often extends to the CMA but also interconnect the PM of each hemisphere. The role of the dorsal part of the PM might be linked to the integration of both limbs into one sequence and the suppression of automated mirror movements. In more demanding coordination tasks activation in the ventral part of PM are also reported (Swinnen et al. 2004).

Previous studies analysing cortical activity related to precision grip did not measure the forces involved or employ electromyography (EMG). Few studies have simultaneously recorded forces and EMG during fMRI. However, cortical activity is related not only to the action realized but also to muscle force and activity (Ehrsson et al., 2000; Ehrsson et al., 2001; Ehrsson et al., 2002; Ehrsson et al., 2003; Kawato et al., 2003). The task realized in these studies was a repetitive task performed without lifting the object or without measuring the applied forces and/or EMG during fMRI.

The first part of chapter IV describes the development of a specific manipulandum and a validated protocol for grip-lift task recordings made simultaneously with EMG and fMRI. The second part of that chapter discusses the effect of the subject’s position and view of the object on precision grip. During fMRI there are position and vision constraints that could influence the performance of a grip-lift task.

I.4. Purpose of the thesis

This thesis aims to evaluate deficits in the grip-lift task in chronic stroke patients and to develop a specific rehabilitation for precision grip in these subjects.

The **second chapter** of the thesis describes deficits in chronic stroke patients in the control of precision grip. As discussed above, various authors have demonstrated grip-lift parameters modifications in stroke patients. In this chapter, the control of precision grip in feedback and feedforward situations are compared with those observed previously in congenital hemiplegia (Bleyenheuft and Thonnard, 2010a).

The **third chapter** describes the rehabilitation program that we created on the basis of data from evidence based therapies. The effect of rhythmic auditory cued grip-lift task oriented rehabilitation in chronic stroke patients is detailed with respect to the three levels of the ICF. Body structures and functions are evaluated through the grip-lift task and the Purdue Pegboard Test, and manual ability and satisfaction with and participation in ADL are quantified with two Rasch-built scales. The Abilhand questionnaire is used to evaluate activity limitations specific to the upper limb (Penta et al., 2001) and the Satis-Stroke Scale to quantify restriction of participation (Bouffioulx et al., 2008). The results of the same therapy in age- and sex-matched elderly subjects are also presented.

To assess more precisely the effect of the training, we developed a fMRI compatible manipulandum presented in **chapter IV**. This setup combined with classical behavioural evaluation methods may allow quantification of the progression of subjects through the “body structures and functions” domain of the ICF. The specificity of fMRI evaluation of the grip-lift task in healthy subjects is presented. The first section is dedicated to the method developed to evaluate grip-lift and first dorsal interosseous muscle activity during fMRI. A description of the technical specification of our fMRI compatible manipulandum highlights the challenge of simultaneously recording grip-lift forces, EMG data for both hands and cortical activity images with accuracy. Additionally, we discuss the analysis of the recorded forces, EMG data and fMRI data.

Finally, all techniques having limitations, the implications of the subjects’ position and view during fMRI must be clarified. In the second part of this chapter, we observe the effect of the supine posture and the lack of a view of the object on grip-lift parameters in healthy adults. Use of fMRI requires that the subject be supine and that his view of the object be restricted. To further employ this method in the investigation of cortical activation in the grip-lift task, this study aims to clarify the possible effect of these constraints on precision grip performance.

The **appendix** presents a triple case report combining the rehabilitation method described in chapter III and the fMRI compatible setup detailed in the first section of chapter IV.

CHAPTER II: Control of precision grip in chronic stroke patients

Abstract

Skilled hand movements require a precise co-ordination between the grip force (GF) and the load force (LF). To coordinate those forces we rely on both a predictive and a reactive control. On the basis of specific impairments observed previously in children with hemiplegic cerebral palsy (HCP), we aimed to assess the predictive or/and reactive nature of hand deficits in stroke patients. This case control study was conducted with 8 stroke patients and 8 control subjects. The load of a handheld object was rapidly increased by dropping a mass attached to the object. We tested predictive and reactive aspects of the movement in the same task since the drop was triggered either unexpectedly by the examiner (reactive condition) or by the patient himself (predictive condition). Deficits observed in the paretic hand were similar to those previously highlighted in children with HCP. Under predictive conditions, temporal deficits were observed after impact. Under reactive conditions, the reflex latency was slightly increased in the paretic hand. The non-paretic hand demonstrated similar results to controls. The predictive mechanism is present but altered in the paretic hand. These alterations suggest an inability to anticipate the consequences of dynamic perturbations in the paretic hand only.

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INTRODUCTION

The manipulation of small objects between the thumb and index finger requires a precise coordination between the grip force (GF) and the tangential load force (LF) (Johansson and Westling, 1984; Johansson and Westling, 1988). This coordination of forces rely on two types of control mechanisms: a predictive control that allows healthy subjects to anticipate movement on the basis of sensorimotor memory and a reactive control that enables correction of the movement through feedback. An internal model in the central nervous system has been suggested to account for the predictive mechanisms (Wolpert and Ghahramani, 2000). Stroke patients usually do not present normal skilled hand movements. They typically exhibit excessive GF and large perturbations in movement timing (Hermsdörfer et al., 2003; McDonnell et al., 2006; Nowak et al., 2003; Raghavan et al., 2006; Takahashi and Reinkensmeyer, 2003). However, it is not clear if their impairments in fine prehension are linked to deficits in predictive or/and reactive control of the movement. The excess of GF has generally been associated with perturbations in sensory feedback, and the disordered timing of the movement is currently attributed to deficits in internal models (Nowak et al., 2003; Takahashi and Reinkensmeyer, 2003). However, perturbations in the timing of the movement could also be due to altered sensory feedback transmission which could prevent updating of the sensorimotor memory. Therefore, it would be interesting to determine the relative contributions of predictive and reactive mechanisms to deficits in precision grip using paradigms in which both can be tested separately.

Such a paradigm has been used for stroke patients in the context of anticipatory postural adjustments (APA) of the arm (Bennis et al., 1996) but never to assess the subtle coordination of forces required to carry out precision grip tasks. In children with hemiplegic cerebral palsy (HCP), both predictive and reactive control have been previously studied, showing impairments in the delays related to both predictive and reactive control (Bleyenheuft and Thonnard, 2010a). In this study the same paradigm, using the brisk loading of a handheld object (in predictable or unpredictable conditions), will be used to investigate the predictive or/and reactive nature of hand deficits in the paretic and non-paretic hands of chronic stroke patients.

METHODS

This study was authorized by the Ethical Committee of the Université catholique de Louvain, Faculty of Medicine in Brussels, Belgium. Eight stroke patients (3 women, mean age: 54.5±11.0) with no or limited cognitive deficits (>26/30 on the MMSE-mini mental state examination) as well as eight matched controls (54.5±10.5) gave their written informed consent and were assessed. Hemiplegia level was categorized with the Stroke Impairment Assessment Scale (SIAS). A brief description of patients is provided (Table II. 1).

Table II.1. Clinical description and lesion description

Patient (sex)	Age (years)	Time since stroke (months)	Clinical description	Lesion description (MRI)	SIAS /76	MMSE /30	Additional Disorders
1 (F)	36	65	R hemiparesis	L sylvian CVA	64	29	slight aphasia
2 (F)	48	124	L hemiparesis	Ablation of R frontal angioma in premotor area	60	30	hemianopsia, tactile detection
3 (F)	49	53	L hemiparesis	R deep sylvian ischemia	60	N/A	
4 (M)	49	18	L hemiparesis	R deep and superficial sylvian CVA, extended to frontal inferior area, insular, temporal and lenticular R areas	66	29	
5 (M)	57	62	L hemiparesis	N/A	48	28	tactile detection
(M)	60	33	R hemiparesis	L deep sylvian ischemia (lenticular nucleus, insula, corona radiata, caudate nucleus)	69	28	
7 (M)	67	7	R hemiparesis	L ischemia in the posterior part of putamen and corona radiata	72	29	
8 (M)	69	110	L hemiparesis	R Large sylvian CVA with wallerian dysgenesis of CST, peduncular atrophy and bulbar olive dysgenesis	70	29	

R=right; L=left, M=male; MRI=magnetic resonace imaging; SIAS=stroke impairment assessment scale; MMSE=mini mental state examination; N/A= not available; CVA=cerebral vascular accident; CST=corticospinal tract; tactile detection=sensory impairment measured with the Semmes-Weinstein monofilaments

Apparatus

A cylindrical object (80mm diameter, 220g) with two parallel force-torque sensors was used. Each sensor provided values of GF and LF,calculated from the three force components (Fx, Fy, Fz). The Fx, Fy, and Fz sensing ranges were ±40,

±40, and ±120N, with resolutions of 0.002, 0.002, and 0.006N, respectively. The horizontal (x) and vertical (y) centers of pressure were also measured. The object was placed on an open table (Figure II.1), and a steel mass (100g) was attached to the object via a Kevlar string. The additional mass could be placed on an electromagnet located a few centimeters above its lowest position, making possible to lift the object without any influence of the additional mass.

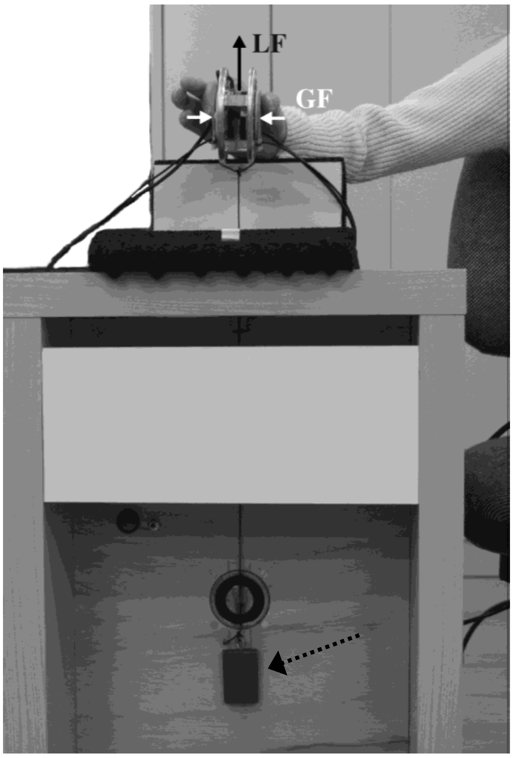

Figure II.1. Handheld object used to measure the different forces during the task. Grip force (GF) normal to the contact surfaces is indicated by white arrows, tangential load force (LF) by a black arrow and the steel mass by a dotted arrow.

Procedure and experimental protocol

Participants were sitting next to a table providing support to their forearm. They were presented with an object and instructed to grasp it and hold it in a standard position. Three different conditions (predictive, unexpected blank and reactive condition) were tested.

For predictive conditions, participants held a button switch in their free hand, which they pressed in response to an auditory signal. This instantly turned off the magnetic field, which caused the mass to drop (4cm), followed by a sudden increase in LF (impact).

Blank conditions were similar to the predictive conditions at the beginning, but the release mechanism was unexpectedly blocked meaning that no drop occurred.

In reactive conditions, the drop of the mass applied to the handheld object was both sudden and unpredictable because the release mechanism was triggered by the examiner.

The dominant hand of control subjects and both hands of stroke patients were systematically tested, beginning with the paretic hand of stroke patients. The use of only one hand in the healthy participants was justified by the absence of difference between both hands of controls in a previous study (Bleyenheuft and Thonnard, 2010a). Each subject performed 35 consecutive trials for each hand according to the following sequence: fifteen predictive trials, five blank trials, five predictive trials and ten reactive trials. The consecutive presentation of the trials in each block allowed us to study the evolution of the motor response within each condition (stimulation predicted, no stimulation, stimulation not predicted). The participants were unaware that a transition between blank and impact trials would occur. As a consequence, trials 1, 16 and 21 were considered catch trials. The coefficient of friction (CF) was measured through eight lift-and-drop maneuvers, which preceded and directly followed the experiment (Bleyenheuft and Thonnard, 2010a).

Data acquisition and analysis

The signals from the force sensors were digitized on-line at 1000Hz with a 12-bit6071E analog-to-digital converter in a PXI chassis (NI, Austin, TX, USA). After analog-to-digital conversion, the GF and GFrate signals were further low-pass filtered with a fourth-order, zero phase-lag Butterworth filter with a cut-off frequency of 25Hz.

The impact phase, defined as the period including the impact time and the modulation of GF preceding and following the impact, was analyzed using the following temporal variables (Figure II.2):

(a) anticipatory delay – the delay between the onset of GF and the impact.

(b) delay post-impact – the delay between the impact and the increase of GF after the impact.

c) delay to GFmax – the delay between the impact and the GFmax.

In addition, dynamic variables were investigated during the impact phase: GF at impact, GFmax and GFrate max before and after impact (Figure II.2). An average GF was also calculated in each trace during the stable phase defined visually before the impact on the LF trace.

The estimate of the impact occurrence (t_0) in blank trials was computed by calculating an average delay between switch and impact for each subject on all impact trials. In blank trials, the average delay for each subject (~200ms) was added to the moment the subject pressed the switch, providing an estimate of the impact occurrence.

For each trial, GFrate max, GFmax, and the impact (LFmax) were detected as the absolute maxima during the impact phase.

The number of slips was counted in both the predictive and reactive trials. A slip was identified during the impact phase when the displacement of the vertical component of the centre of pressure (y) was higher than 5mm.

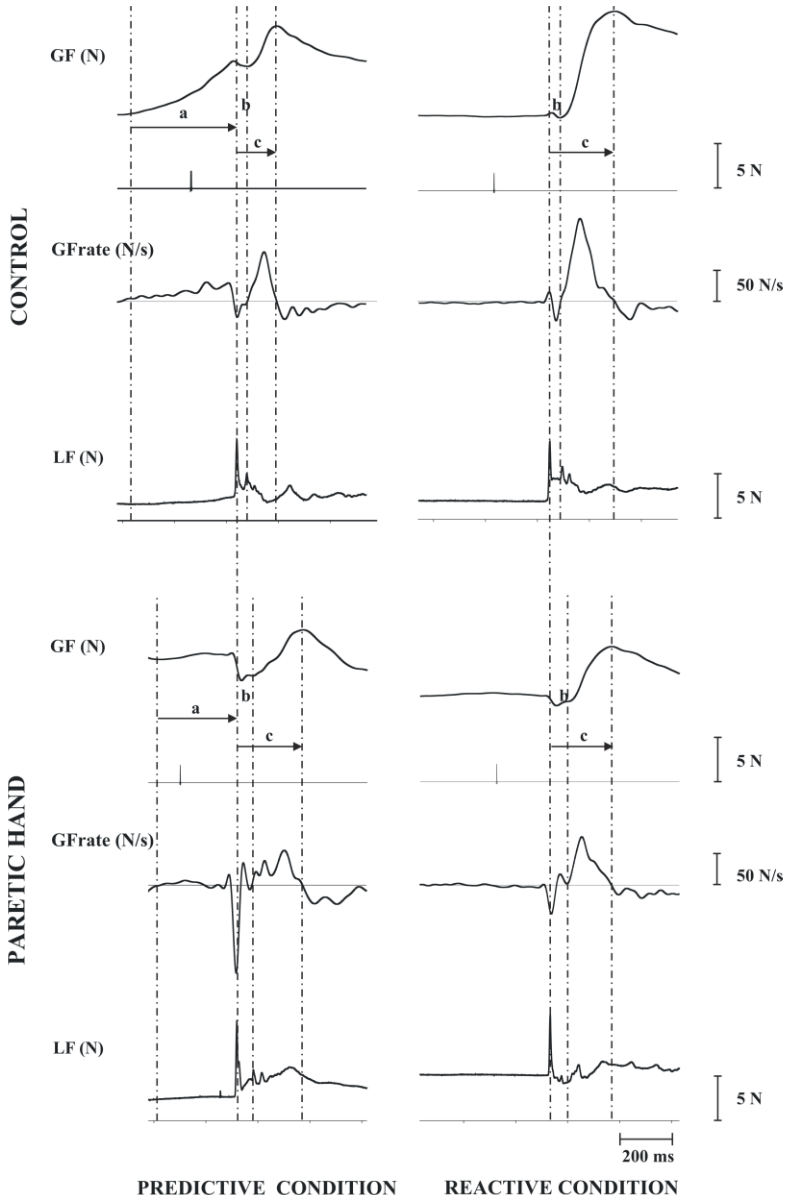

Figure II.2. Traces from a control and a stroke patient. Examples of GF, GFrate and LF traces recorded under predictive and reactive conditions from a control and a stroke patient. In each trace, vertical dotted lines represent time points used to calculate the different delays. (a) is the anticipatory delay, (b) is the delay post-impact, (c) is the delay to GFmax. The short vertical bar under the GF traces represents the moment the subject pressed the button-switch. The auditory cue is not represented here since it arises previously. In the predictive condition, stroke patient trace presents a small slip inducing a difference of 2mm between the center of pressure before and after impact. This slip is shown in this example by a slight decrease in GF and a negative GFrate at the moment of the impact. However, since no drop of the object was observed, this was not considered as a failure in the task.

Statistics

Previous studies (Bleyenheuft and Thonnard, 2010a; Bleyenheuft and Thonnard, 2010b), showed that one trial was sufficient to get stable values for all variables studied. Therefore in subsequent analysis, mean values excluded the 1st trial of each sequence.

ANOVA (or Kruskall-Wallis test for non-parametric conditions) was performed to compare the three groups of data, (paretic and non-paretic hands of stroke patients and dominant hand of control subjects) in each condition (predictive and reactive). A Tukey pairwise multiple-comparison procedure, including an automatic p-value correction, determined which groups were significantly different.

A repeated measure ANOVA on ranks was performed on the first 25 trials of all participants to detect trial-to-trial differences, as well as changes due to blank trials in the sequence. This analysis was conducted separately for data from each condition. Post-hoc analysis was conducted using Tukey tests.

RESULTS

Predictive and reactive conditions

Figure II.2 illustrates typical traces from trials involving a control participant (top panel) and trials in which the paretic hand of a stroke patient (lower panel) was tested under predictive (left) and reactive (right) conditions.

As previously described (Bleyenheuft et al., 2009), during predictive conditions control subjects demonstrated an increase in GF that preceded the impact, and a second GF increase (that led to maximum GF) after the impact. In reactive conditions, the GF of the control subject was stable prior to the impact. A rapid GF increase that led to GFmax was induced by the impact.

In stroke patients, under predictive conditions the paretic hand exhibited an anticipatory delay that was similar to those observed in control subjects, but the GFrate max was significantly lower than that of control subjects. The post-impact rise in GF that leads to GFmax is also present in the paretic hand, but both the onset and maximum occur after a longer delay than in controls. As expected, under reactive conditions, stroke patients presented a rapid GF increase that followed the impact. In the paretic hand, this elevation in GF had a slightly later onset but reached GFmax within a similar time to controls.

In the non-paretic hand, variables measured were similar to those observed in the controls (see Table II.2).

Table II.2. mean values of dynamic and temporal variables

Variables	**Values**			**P value**	**Post-hocs**		
	Paretic Mean (SD)	**Nparetic** Mean (SD)	**CTRL** Mean (SD)	**ANOVA or Kruskall-W**	**Paretic / Nparetic**	**Paretic / CTRL**	**Nparetic / CTRL**
Predictive condition							
GF stable phase (N)	11.2 (5.84)	10.7 (4.17)	8.3 (4.41)	p=0.225			
GF at impact (N)	12.8 (6.58)	15.7 (4.90)	15.4 (6.39)	p=0.575			
GF max (N)	16.1 (6.83)	22.2 (6.17)	21.7 (6.71)	p=0.140			
Gfrate max before I (N/s)	15 (9.8)	30 (23.3)	38 (16.5)	p=0.045*	p=0.229	p=0.038	p=0.0613
Gfrate max after I (N/s)	69 (45.2)	118 (49.5)	108 (43.4)	p=0.106			
D anticipation (ms)	359 (30)	329 (75)	376 (82)	p=0.185			
D post-impact (ms)	71 (22)	51 (9)	43 (7)	p=0.003*	p=0.028*	p=0.002*	p=0.533
D to GF max (ms)	283 (150)	186 (58)	160 (29)	p<0.001*	p<0.001*	p<0.001*	p=0.649
Reactive condition							
GF stable phase (N)	11.9 (5.82)	11.2 (4.78)	10.1 (5.41)	p=0.505			
GF at impact (N)	12.1 (5.41)	11.5 (5.41)	10.6 (5.96)	p=0.862			
GF max (N)	17.2 (7.22)	20.8 (7.61)	21.6 (6.94)	p=0.475			
Gfrate max after I (N/s)	85 (52.8)	117 (41.9)	144 (42.4)	p=0.073			
D post-impact (ms)	71 (18)	57 (13)	52 (11)	p=0.026*	NS	S	NS
D to GF max (ms)	266 (98)	243 (66)	230 (34)	p=0.596			

CTRL=control subjects; Nparetic=non-paretic hand; Kruskall-W=Kruskall Wallis; D=delay
Results of Tukey tests (post-hoc) were given as p values in ANOVA and by letters (S=significant, NS=nonsignificant) for Kruskall-Wallis, * indicates significant difference

Table II.2 summarizes the mean values of the variables in stroke patients and control subjects. Under predictive conditions, there were significant differences between the paretic hand of stroke patients and control subjects in the defined primary variables. First, the post-impact delay was significantly longer in the paretic hand of stroke patients. Second, the delay to GFmax was more prolonged and showed greater variability (coefficient of variation: 851±215%, mean±SD) in the paretic hands of stroke patients than in either controls (36±11%) or the non-paretic hands of patients (29±23%). This indicated an inconsistent (less regular) temporal adjustment in reaching the GFmax under predictive conditions (Kruskall-Wallis, H=14.2, 2DF, $p<0.001$). In addition, before the time of impact the GFrate max was significantly reduced in the paretic hand of stroke patients. Post-hoc analysis showed that the non-paretic hand did not present significant differences with the dominant hand of controls.

Under reactive conditions, the post-impact delay was significantly longer in the paretic hand of stroke patients than in controls. This delay was also more variable in the paretic hand (coefficient of variation: 36±19%) than in controls (21±12%). Neither the delay to GFmax (Table II.2), nor the variability (Kruskal-Wallis, H=2, 2DF, $p=0.369$) were significantly increased in the paretic hand of stroke patients compared to controls.

The coefficients of friction (CF) of stroke patients were not significantly different from those of controls (RM ANOVA, $p=0.925$). The number of trials during which a slip occurred was significantly higher in the paretic hand of stroke patients (11.5±11% of the trials) when compared to control values (4±4.3%), but only under predictive conditions (Kruskal-Wallis, H=7.74, 2DF, $p=0.021$). Post-hoc analysis showed that the percentage of slips on the non-paretic hand (5.5±6.7%) did not differ from control values.

The use of blank trials

CONTROLS

As illustrated in Figure II.3A, the mean GFmax was significantly lower during all blank trials except on the first (RM ANOVA, F=7.8, 24DF, $p<0.001$). This first blank trial (trial 16) was not significantly different from the preceding impact trials (Tukey test; $p>0.05$). The second blank trial (17) was significantly different from trials 2 to 7. The third blank trial (18) was significantly different from trials 2 to 15. The 4th and 5th blank trials (trials 19 and 20) were significantly different from trials 2 to 15 and 21 to 25 (all $p<0.05$).

The delay between the impact and GFmax was not significantly different between impact trials (160±29ms) and blank trials (145±34ms). The very first trial tended to present a longer delay (287±158ms; Friedman analysis, χ^2=34.3, 24DF, p=0.079).

PARETIC HAND

Surprisingly, the mean GFmax of paretic hands (Figure II.3B) was not significantly lower during blank trials (RM ANOVA, F=1.2, 24DF, p=0.279). Due to the large intra- and inter-subject variability, there was no significant difference in the delay to GFmax in impact trials (278±116ms) compared to blank trials (-49±365ms). During blank trials, there were typically shorter delays to GFmax or even negative delays to GFmax (GFmax occurred before the expected impact).

NON PARETIC HAND

Results obtained from the non-paretic hand of patients were similar to those of controls. For example, the mean GFmax (Figure II.3C) was significantly lower during all blank trials (RM ANOVA, F=2.9, 24DF, p<0.001) except on the first two trials (trial 16 and 17). These initial blank trials were not significantly different from the preceding impact trials (Tukey test; p>0.05). Trial 18 to 20 were significantly different from other impact trials (all p<0.05). As in controls, the delay between the impact and GFmax was not significantly different for impact trials (186±58ms) compared to blank trials (175±101ms; Friedman analysis, χ^2=34.3, 24 DF, p=0.501). The very first impact trial did not present a longer delay.

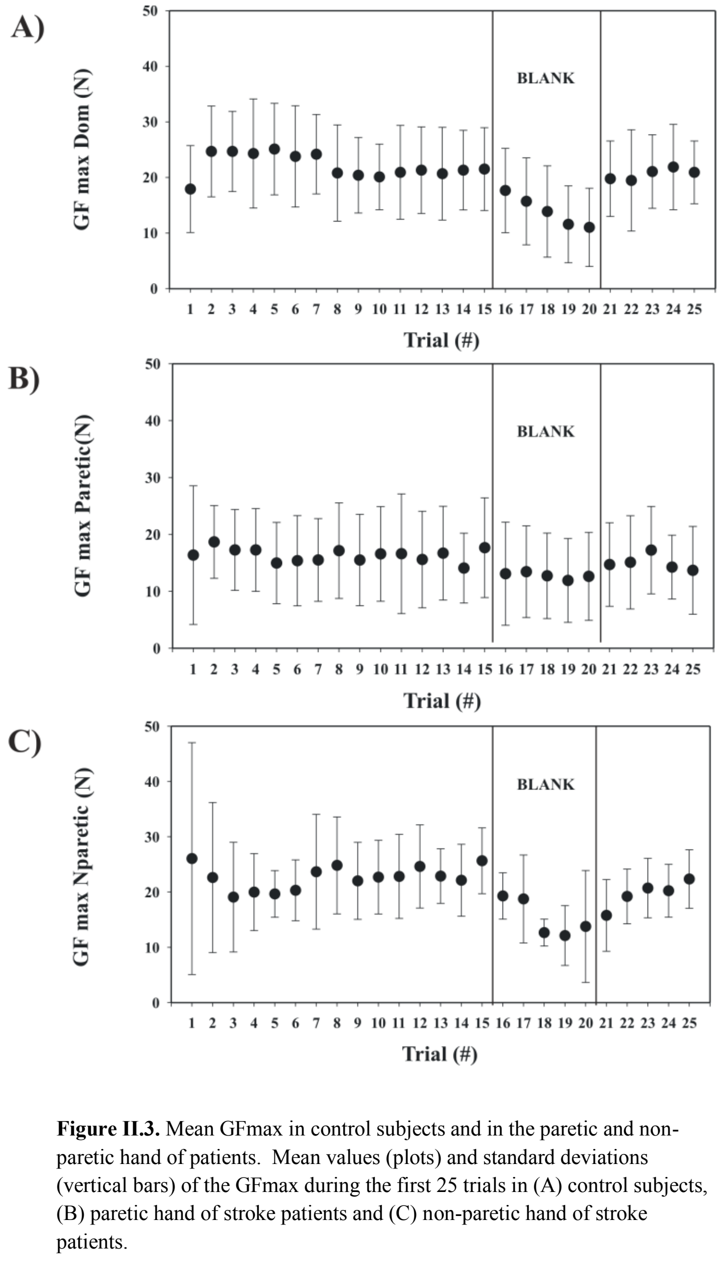

Figure II.3. Mean GFmax in control subjects and in the paretic and non-paretic hand of patients. Mean values (plots) and standard deviations (vertical bars) of the GFmax during the first 25 trials in (A) control subjects, (B) paretic hand of stroke patients and (C) non-paretic hand of stroke patients.

DISCUSSION

In this study, we investigated whether impaired precision grip of stroke patients resulted from deficits in the ability to anticipate movements and/or to perturbations in reactive loops. Significant perturbations of predictive regulation were observed for the delay to GFmax, the post-impact delay. In reactive control, deficits were limited to the post-impact delay. Under predictive conditions the GFrate max was also altered and more slips were observed in the paretic hand of stroke patients. In addition, the non-paretic hand exhibited performances similar to controls under both predictive and reactive conditions.

The longer post-impact delay under both conditions, as well as the lower GFrate max of the paretic hand were likely linked to muscular modifications. It is well-known that many patients suffering from stroke exhibit muscle weakness (Bohannon, 2007). This weakness could be linked to a loss of functioning motor units (Arasaki et al., 2006) or to a selective affectation of the large motor units with a high threshold (Lukács et al., 2008). These muscular alterations are likely to affect the development of force, since the recruitment of new motor units according to increasing size is one of the mechanisms used to increase one's force output (Henneman and Olson, 1965; Henneman et al., 1965a; Henneman et al., 1965b).

Muscular modifications are also most likely responsible for the longer post-impact delay under both conditions. This delay is either wholly (under reactive conditions) or partly (under predictive conditions) due to the latency of a stretch reflex induced by the impact. In view of the defined order with which motor units that innervate different types of fibers are recruited (Calancie and Bawa, 1984), the selective affectation of large, high-threshold motor units (Lukács et al., 2008) could provide an explanation for the increased lag in the post-impact delay under both conditions.

However, the longer and more variable delay to reach GFmax cannot be related to these muscular modifications. A purely muscular phenomenon should have induced the same perturbations under both predictive and reactive conditions and no changes in the delay to GFmax could be identified under purely reactive conditions. Therefore, this delay is likely to be impaired under predictive conditions because of higher-order perturbations. It has recently been demonstrated in self-triggered impulsive loading tasks that the increase in GF arising after impact is intrinsically of a predictive nature (Bleyenheuft et al., 2009). This last part of the trace would be planned in advance: a moderate GF at impact would be used to dampen the collision and an increase in force would be developed afterwards to stabilize the object. The different time taken to reach GFmax in the paretic hand is thus evidence of an important perturbation of predictive control in the paretic hand of stroke patients. This is further supported by the variability of the temporal adjustment of this delay, which indicates either an inability to reproduce a motor plan or an inability to form it in the first place. The disordered nature of this delay was probably responsible for the larger number of slips observed in the paretic hand of stroke patients under predictive conditions. Interestingly, slips were no more prevalent in the paretic hand under reactive conditions. The hypothesis of a high-order motor planning deficit in predictive conditions is further supported by the lack of decrease in GFmax for blank trials completed with the paretic hand. On the paretic hand, patients were not able to regulate the amplitude of GFmax to the different conditions. This deficit in GF regulation and in the timing to reach the maximum (D to GF max) strongly suggests impairments in predictive control. Altogether, these results, acquired in chronic patients with cortical and subcortical lesions, are consistent with high–order motor planning deficits in skilled hand movements, probably due to deficits in the implementation of internal models. This is consistent with previous studies. In acute stroke patients performing point-to-point movements with handheld objects, deficits were observed in prediction of the inertial load profile (Nowak et al., 2003). Identical perturbations were demonstrated by patients with cortical and subcortical lesions suggesting that an internal model responsible for the precise regulation of forces was perturbed. While internal models are believed to be formed in the cerebellum (Wolpert and Flanagan, 2001; Wolpert et al., 1998), the authors suggested that cortical and subcortical structures could be involved in the subsequent processing of motor commands. The ability to learn anticipation has also been studied in chronic patients by applying forces to the patient's arm while they tried to reach a target (Takahashi and Reinkensmeyer, 2003). It was also concluded that implementation of internal models is impaired in patients with cortical and subcortical lesions, although an incomplete ability to form and use internal models remains. It is of great interest that the high–order motor planning deficits observed in the paretic hand of stroke patients with subcortical problem can be corrected by transferring information from the unaffected hand –at least in right hemiparesis (Raghavan et al., 2006).

This last study is of particular interest since we show here that the management of a rapid increase in forces is preserved by the non-paretic hand of stroke patients. The non-paretic hand is thus likely to be used to form a correct internal model with the relevant information being used for the benefit of the paretic hand. This argues in favor of an alternate use of both hands in rehabilitation programs starting with the non-paretic hand to implement a correct planning of movement in the paretic hand. Interestingly, this is reinforced by the consistence of these results with previous results obtained in the same task for children with HCP (Bleyenheuft and Thonnard, 2010a). The potential use of the non-paretic hand to form correct internal models is further supported by the results obtained when performing blank trials. Similar to healthy control subjects, the non-paretic hand of stroke patients demonstrated both an ability to adapt the amplitude of GFmax as a function of previous trials and also constancy in the delay to reach GFmax, which indicated the predictive nature of this late GF increment (Bleyenheuft et al., 2009). In contrast, such predictive planning could not be observed in the paretic hand, as proven by the lack of adaptation of GFmax to previous trials and the high variability of the delay to reach GFmax under both impact and blank conditions.

CHAPTER III: Precision grip rehabilitation in chronic stroke patients

Abstract

Most chronic stroke patients present difficulty in the manipulation of objects. The aim of this study was to test whether an intensive program of precision grip training could improve hand functioning of patients at more than six months after a stroke. This was a cross-over study, hence at inclusion the patients were randomly divided into two groups: one group started with the bilateral movement therapy and the other one started with the unilateral movement therapy. The subjects were assessed on four separate occasions across a 12 week period; (a) at inclusion to the study, (b) four weeks later, immediately before the first rehabilitation session, (c) after four weeks of one therapy, and (d) after a further four weeks of the other therapy. Ten patients completed two consecutive four-week sessions (1 h, 3 d/w) of therapy. The therapy comprised unilateral and bilateral repetitive grip-lift task oriented rehabilitation with rhythmic auditory cueing. The grip-lift force coordination, digital dexterity, manual ability and the level of satisfaction (with activities and participation) were assessed.

A one way RM ANOVA across the four evaluations did not detect any objective improvement of the measured variables after eight weeks of specific intensive training. Precision grip training was shown to not generate significant improvement in grip-lift task, digital dexterity, manual ability or satisfaction in chronic stroke patients.

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INTRODUCTION

Hands are essential for the dexterous manipulation of objects in activities of daily life (ADL). Following stroke the ability to hold an object between the thumb and index finger can be impaired due to limitations in sensitivity, force and digital dexterity.

The grip-lift task analysis procedure provides a means to objectively quantify the way an object is taken between the thumb and index finger (Westling and Johansson, 1984). Dynamic and temporal variables are usually used to study the perpendicular (grip force, GF) and tangential force (load force, LF) to the contact surfaces. In stroke patients some of the grip-lift variables are modified (Mc Donnell et al., 2006).

A range of different therapies have obtained satisfactory results for the upper limb motor recovery in chronic stroke patients (Nowak and Hermsdorfer, 2009; Shi et al., 2011). For example, constraint-induced movement therapy (CIMT) involves treatment mechanisms that are supported by established behavioral learning theory and evidence of brain plasticity (Sterr and Saunders, 2006).

In contrast, because stroke induces also reorganization in contralesional motor networks, repetitive bilateral training is being increasingly used. This intracortical inhibition and facilitation therapy uses a rhythm based auditory cue to prompt the realization of bilateral functional tasks or repetitive arm movements (Whitall et al., 2000; McCombe Waller et al., 2008).

Hence, interest in establishing the effectiveness of a treatment that combines both unilateral and bilateral therapies is justified. However, both therapies focus on global upper limb movement exercises with the primary aim to recover proximal joint control. Indeed, the spontaneous upper-limb recovery usually shows a proximo-distal gradient. Furthermore, current guidelines for the design of post-stroke upper limb rehabilitation programs also emphasize the importance of promoting distal motor capacities (Oujamaa et al., 2009). Therefore, in the current study we focused on developing a modification of the two bilateral and unilateral therapies, specifically targeting the distal extremity of the upper-limb, for the rehabilitation of precision grip. First, we tested unilateral exercises based on the CIMT theory of forced–use. Second, we tested bilateral arm training exercises with rhythmic auditory cueing facilitation. To our knowledge, the current study is the first to focus on the recovery of precision grip capacity, taking into consideration grip-lift parameters by means of a repetitive unilateral and bilateral grip-lift task-oriented rehabilitation procedure with rhythmic auditory cueing in chronic stroke subjects.

The aim of this study was to test whether such a precision grip rehabilitation program could improve hand function of patients at more than six months after a stroke.

METHODS

The protocol of this study was approved by the School of Medicine Ethical Committee of the Université catholique de Louvain (Belgium). All subjects gave their written informed consent.

Subjects

Ten chronic hemiparetic subjects (mean age 66 ± 11.1 years, 9 male and 1 female) were initially allocated to the treatment. To be included to the study, the subjects had to have had a single first stroke (evidenced by MRI) a minimum of six months before participating in the study. All subjects had completed a neurological clinical evaluation proving hemiparesis by means of the Stroke Impairment Assessment Set (SIAS) (Liu et al., 2002; Chino et al., 1996). The subjects had to be able to lift and hold an object of 250gr between the thumb and index finger for a few seconds. A mini-mental state evaluation (MMSE) was conducted, in which the subject had to score above 26/30, which implied a capability to understand the injunctions and respond to self-reported questionnaires. Subjects with other upper-limb pathologies were excluded.

In addition, eight healthy control subjects (mean age 73 ± 9.1 years) completed the evaluation on one occasion, in order for comparison of their results to those of the chronic stroke subjects.

Protocol

An independent evaluator, who operated under ‘blind’ conditions with respect to the treatment allocation of each of the subjects, was designated to assess the upper limbs, starting with the non-paretic hand.

The subjects were assessed on four separate occasions across a 12 week period. The first assessment (t_0) was conducted when the subject was first included in the study. The second assessment (t_1) was made after a period of four weeks, during which time the subject did not receive any specific treatment. This allowed for comparison between t_0 and t_1 confirming that the subjects were in a chronic phase with no spontaneous recovery of the upper limbs function. The third evaluation (t_2) was made four weeks later, during which time the patient had completed the first half of the specific grip-lift task oriented rehabilitation. The final evaluation (t_3) was made after another four weeks, following the completion of the second half of the specific grip-lift oriented rehabilitation program.

This was a cross-over study. Hence, at inclusion the patients were randomly divided into two groups: one group started with the bilateral movement therapy and the other one started with the unilateral movement therapy. After the first four weeks of intensive rehabilitation (i.e. at t_2), the two groups swapped (i.e. ‘crossed over’) to complete a further four weeks of the alternate therapy type. The therapy sessions occurred for a period of one hour, three times a week for eight weeks (i.e. four weeks of bilateral movement therapy and four weeks of unilateral movement therapy). For the entire period of the program, ongoing treatments were kept unchanged.

Rehabilitation intervention

Bilateral movement therapy

Seven bilateral grip-lift task-oriented exercises with auditory cueing were performed in a random order. The bilateral movement therapy comprised four simultaneous bilateral exercises (Fig. III.1A-D) and three alternated bilateral movements (Fig. III.1E-G). All exercises were specifically oriented on the grip-lift task.

Each exercise, except for task 3 (oscillation task, Fig. III. 1C), was auditory cued. The rhythm (speed of cueing) was selected as the maximal rhythm required by the subject to properly execute the task beforehand during a test trial (minimum 24bpm). The rhythm and level of difficulty were adapted across the sessions to encourage improvement in patient performance.

Unilateral movement therapy

Unilateral movement therapy comprised the same exercises that are described in the bilateral movement section above. However, each task was completed exclusively with the paretic hand of the subject. The rhythm and task difficulty level were also adapted across the sessions to encourage improvement in patient performance.

Figure III.1. Grip lift orientated bilateral movement therapy comprising four simultaneous bilateral tasks (A, B, C and D) and three alternated bilateral movements tasks (E, F and G). (A) Simultaneous pile up task. (B) The subject was required to remove and replace blocks from the four horizontal branches of a tree-like apparatus, with both hands simultaneously. (C) Simultaneous bilateral oscillation task at a spontaneous rhythm. (D) This task required the subject to, simultaneously with both hands, separate and then rejoin two rows of blocks. (E) Tower building one hand after the other. (F) Blocks of decreasing size were placed on a wooden stem by one hand after the other. (G) Copying a drawing with the same blocks to be placed with one hand after the other.

International Classification of Functioning, Disability and Health (ICF) based Upper limb assessment

Body structures and functions

The subjects were seated on a chair in front of a table to complete the grip-lift tasks. The procedure for each task was explained carefully, step by step, and demonstrated to each subject before each evaluation. An opportunity to practice each task was given before being officially assessed. Subjects were required to grasp a manipulandum between the thumb and index finger (Figure III.2A), lift it of the table, hold it for about 10s and replace it on the table. Each subject performed six of these grip-lift trials with each hand, starting with the non-paretic hand.

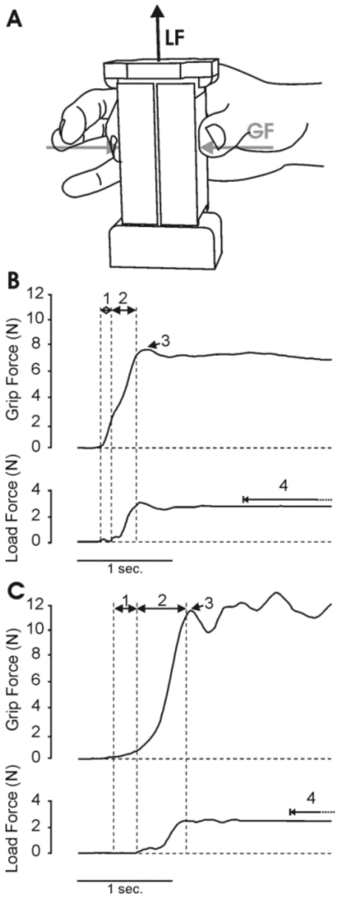

Figure III.2. (A) Diagram of the manipulandum held between the thumb and index fingers. Light grey arrows indicates the grip force (GF) while the black arrow indicates the load force (LF) exerted on the contact surfaces. (B) Typical trace of a grip-lift trial realized with the dominant hand of a healthy subject. (C) Paretic hand, of a chronic stroke subject, grip-lift trial typical trace. Both traces (B-C) indicate the preloading phase (1), the loading phase (2), the GF peak (3), and part of the stable phase (4).

The manipulandum was instrumented with full Wheatstone Bridges incorporating three strain gauges to allow the force perpendicular to each contact surface to be measured (GF left and GF right), in addition to the total tangential force applied on the object (LF). Each sensor used a binocular design of yield strength 300 N. The manipulandum was calibrated to a maximum scale of 30N in each direction, and demonstrated a maximum nonlinearity of 0.70 and 0.35 percent of full scale for the LF and both GF directions, respectively. The analogue signals were amplified and filtered using a four-pole–Bessel filter, with a low-pass 150Hz cut-off filter and then sampled at 2000Hz with a 16-bit resolution. The data were stored for off-line analysis. Typical traces of grip-lift trials for a dominant hand of a healthy subject and the paretic hand of a chronic stroke subject are shown in Figure III.2.

The following parameters were measured from the force traces (Figure III.2B-C) (McDonnell et al., 2006; Duque et al., 2003): (1) the preloading phase, i.e. the delay between the onset of GF and the onset of LF (threshold 0,1N), (2) the loading phase, i.e. the delay during which both GF and LF increased until LF equaled the weight of the manipulandum (2,75N), (3) GF_{max}, i.e. the maximum GF when the object was lifted off the table, (4) the hold ratio, i.e. the mean GF/mean LF during the stable phase which was started a minimum of 1 s after the GF_{max} was reached, and which lasted for a duration of at least 2s. Additional parameters were extracted from the first derivative of GF and LF during the preloading and loading phase, including: (a) the mean GF rate, which was calculated between the onset and the peak of GF (dGF/dt), and (b) the peak GF rate. The precise synergy between GF and LF was calculated for each trial by means of a cross-correlation function between dLF/dt and dGF/dt. To determine the larger coefficient of correlation between the two signals, one signal was shifted with respect to the other by steps of 2.5ms. This method provided two values for each trial: (a) the maximum coefficient of correlation, which indicates the similarity between the profiles of the force rates, and (b) a time-shift, which indicates the asynchrony between dGF/dt and DLF/dt (Duque et al., 2003).

The Purdue pegboard test was used to evaluate the digital dexterity (Desrosiers et al., 1995; Tiffin and Asher, 1948). Both hands were each tested three times, with the final score being expressed as the mean of the number of pegs that were picked up from a cup and inserted into the holes of the board within a 30s period.

Activity and Participation

The capacity to manage ADL requires the use of the upper limbs, which is termed manual ability, whatever the strategy involved. This parameter was assessed using the ABILHAND questionnaire (Penta et al., 2001).

Subject satisfaction with activities and participation in daily life

The SATIS-Stroke questionnaire was used to measure an individual's own perspective of their performance in daily activities and participation in real-life situations with respect to their own needs, which does not necessarily relate to the actual level of difficulty of performing the activity or life situation (Bouffioulx et al., 2008).

Both the ABILHAND and SATIS-stroke questionnaires were self-reported and the results were expressed as logit scores.

Statistical analyses

The results at t_0 were excluded of our analysis since no significance differences were observed between t_0 and t_1 (paired t-test). A two way RM ANOVA was applied to the results of the paretic hand, at t_1, t_2 and $t_{3,}$ observing the respective effects of unilateral and bilateral therapy. A one way repeated measure analysis of variance (One way RM ANOVA) was used to compare the evolution of the paretic and non-paretic hand of each patient across each evaluation. At t_1, paired t-tests were used to compare: (a) the difference between the non-paretic and paretic hand, and (b) the difference between the paretic hand of chronic stroke subjects with respect to the non-dominant hand of healthy controls. Statistical significance was recognized when $p < 0.05$.

RESULTS

Pre-rehabilitation assessment

An overview of the initial evaluation status of the 10 subjects that participated in the study is provided in Table III.1. The results of the neurological evaluations indicated a broad variation in the SIAS tests of the hemiparetic limb, with scores in the range of 60-75 (out of 76) as a result of a subcortical stroke. It was found that all subjects exhibited a moderate level of hemiparesis, with proprioception impairments being absent in the thumb and index fingers. Nevertheless, the digital dexterity (Purdue Pegboard test) was significantly impaired for the paretic hand compared to the non-paretic hand or controls ($P<0.001$).

Table III.1. Summary of the pre-study (t_0) evaluation results for the 10 chronic stroke subjects

Patient (sex)	Age (years)	Group	Hemiparetic side	MMSE /30	SIAS /76	Lesion description (MRI)	Time since stroke (months)
1 (M)	53	A	Right	28	64	Left thalamic stroke	37
2 (M)	75	B	Right	28	67	Left ischemic capsulolenticulostriated stroke	37
3 (M)	60	A	Right	29	69	Left deep sylvian stroke (extended on M1)	33
4 (M)	69	B	Left	28	67	Right deep and superficial sylvian stroke	111
5 (M)	81	A	Left	27	61	Right basal pontic ischemia	10
6 (M)	67	B	Right	29	72	Left deep sylvian stroke	7
7 (M)	49	A	Left	30	66	Right deep and superficial sylvian stroke	18
8 (M)	67	B	Left	26	60	Right deep sylvian stroke	6
9 (F)	81	A	Right	29	67	Left lenticulostriated stroke	12
10 (M)	58	A	Right	28	75	Left thalamic stroke	8

MMSE = mini-mental state evaluation; SIAS = stroke impairment assessment set; MRI = magnetic resonance imaging; N/A = not available; M = male; F = female; Group A = starting with unilateral movement therapy; group B = starting with bilateral movement therapy

Effect of rehabilitation

Table III.2 presents the results of the paretic and non-paretic hand assessment of the 10 stroke patients before rehabilitation at t_1 and the non-dominant hand of healthy controls. In healthy controls, comparison between the dominant and the non-dominant hand showed no significant difference (P >0.104 in all instances). For this reason, only the results of the non-dominant hand of control subjects were presented in table III.2. In chronic stroke subjects, the temporal grip-lift parameters tended to take longer, however only the loading phase showed a significant difference between both hands (*P* = 0.048). Surprisingly, the grip-lift dynamics (GF_{max} and hold-ratio) showed no significant difference between the paretic and the non-paretic hand (*P* > 0.507 in all instances). However, a high significant difference was detected for digital dexterity (*P* < 0.001). Comparison between the results of the paretic hand of chronic stroke subjects and the non-dominant hand of healthy controls showed a significant difference for the loading phase (*P* = 0.033), the cross-correlation coefficient (*P* = 0.009) and digital dexterity (*P* < 0.001).

Table III.2. Comparison of the grip-lift parameters and the digital dexterity between the non-paretic (NP), paretic (P) hand of chronic stroke subjects and the non-dominant hand of healthy controls (ND) at t_1

	Subjects (n=10)			Controls (n=8)	Subjects vs. Controls
Body structure and function	Non-paretic hand (NP)	Paretic hand (P)	p-value	Non-dominant hand (ND)	P vs. ND p-value
Grip-lift parameters					
Preloading phase (ms)	248 (190.7)	383 (358.9)	0,329	172 (64.2)	0,312
Loading phase (ms)	312 (86.6)	465 (204.8)	0.048*	282 (82.3)	0.033*
GF max (N)	11 (8.5)	12 (5.6)	0,784	9 (4.3)	0,186
Hold ratio (GF/LF)	4.7 (5.2)	3.8 (1.66)	0,507	2.8 (1.77)	0,225
cross-correlation coefficient	0.79 (0.121)	0.75 (0.147)	0,601	0.92 (0.05)	0.009*
Time-shift (ms)	69 (47.7)	86 (55.8)	0,479	70 (42.4)	0,506
Digital dexterity (n)	12 (1.5)	5 (4.1)	<0.001*	13 (2)	<0.001*

Mean (SD), * = significant, NP = non-paretic hand, P = paretic hand, ND = non-dominant hand

Comparison of the t_0 and t_1 results, in chronic stroke subjects, did not show any significant difference. This confirmed that the stroke patients were in the chronic phase with no spontaneous recovery.

The two way RM ANOVA applied to the results of the paretic hand at t_1, t_2 and t_3 did not detect any difference between the bilateral and unilateral movement therapies ($P > 0.144$ in all instances). Given those results, a one way RM ANOVA was used to quantify the evolution of paretic hand capability following eight weeks of specific grip-lift task therapy (Table III.3). There was no significant change found for the body structures and functions [grip-lift parameters ($P > 0.193$ in all instances), digital dexterity ($P = 0.193$)], manual ability ($P = 0.072$) or subject satisfaction with activities and participation in daily life ($P = 0.261$). Furthermore, there was no significant difference in comparisons between the bilateral and the unilateral movement therapies for either of the paretic and non-paretic hands of the subjects ($P > 0.144$ in all instances).

Table III.3. Evolution of the paretic hand grip-lift and dexterity during rehabilitation of the 10 chronic stroke subjects at the inclusion to the study (t_0), four weeks later, immediately before the first rehabilitation session (t_1), after four weeks of the first exercise type (t_2), and after a further four weeks of the second exercises (t_3)

	t_0	t_1	t_2	t_3	p-value
Body structure and function					
Grip-lift parameters					
Preloading phase (ms)	965 (1758.3)	383 (358.9)	612 (640.5)	538 (497.4)	0.453
Loading phase (ms)	385 (110)	465 (204.8)	439 (194.7)	467 (193.7)	0.354
GF max (N)	11 (5.2)	12 (5.6)	11 (5.7)	11 (3.8)	0.497
Hold ratio (GF/LF)	3.5 (1.8)	3.8 (1.66)	4.1 (1.89)	3.4 (1.25)	0.794
cross-correlation coefficient	0.72 (0.169)	0.75 (0.147)	0.72 (0.213)	0.77 (0.161)	0.274
Time-shift (ms)	106 (43.7)	86 (55.8)	94 (48.0)	93 (60.3)	0.749
Digital dexterity (n)	4 (3.8)	5 (4.1)	5 (4.1)	5 (3.9)	0.193
Activity limitation					
Manual ability (Logits)	1.4 (2.06)	1.9 (2.06)	1.8 (1.91)	2.2 (2.02)	0.072
Satisfaction					
Satisfaction in activities and participation (Logits)	1 (1.47)	0.6 (1.13)	0.9 (1.39)	1.0 (1.76)	0.261

Mean (SD)

DISCUSSION

Comparison of the ability of the paretic and non-paretic hands of stroke patients before the onset of therapy showed a significant difference for digital dexterity and for the loading phase during the grip-lift task. Surprisingly, few parameters of the grip-lift task were disturbed in the paretic hand, whereas only the digital dexterity of the paretic hand was markedly impaired. A similar study (McDonnell et al., 2006) reported a correlation between grip-lift capabilities, measured within six months of a stroke, and the overall upper limb function (Action Research Arm Test, ARAT) (Hsieh et al., 1998). That study evidenced significantly longer preloading phases, greater minimal negative loads before lifting the object, and smaller cross-correlation coefficients for the paretic hand.

In contrast, chronic stroke subjects in this study presented a longer loading phase with the paretic hand, which was also significantly different to the duration of this phase obtained for the healthy control subjects. During the loading phase, GF changed in parallel to the applied load, following a forward sensorimotor program (Hermsdorfer et al., 2003; Johansson, 2002). Quantification of the observed parallel change in GF and LF, using the cross-correlation coefficient, indicated that the chronic stroke subjects in our study showed no significant difference between both hands. However, this correlation was significantly smaller to that recorded for the healthy subjects, suggesting that both hands may in fact be affected to varying degrees in chronic stroke patients. This theory has been confirmed in studies where both hands were impaired after unilateral sub-cortical or cerebellar lesions (Anens et al., 2010; Immisch et al., 2003; Nowak et al., 2007a). In these studies, modification of the cross-correlation coefficient was not associated with a higher time-shift, suggesting that the principal functions of forward models were preserved. Similarly negligible time-lags were found by Hermsdörfer et al. (2003) for cerebral chronic and acute stroke patients, which were considered to be the result of a reasonable motor command, whereby the adjustment of GF was synchronized with arm movement in vertical cyclic oscillation movements.

The choice to compare the paretic hand of the patients with the non-dominant hand of controls is related to the fact that the paretic hand often becomes an assisting hand after stroke. Some authors present significant lower impairments in patients with the dominant hand affected compared with the non-dominant hand.

However, there was no effect of dominance on paretic arm use, motor function or performance in activities of daily living at least before a rehabilitation period (McCombe Waller and Whitall, 2005; Harris and Eng, 2006).

In a meta-analysis of stroke patients participating in augmented exercise therapy, no significant summary effect size of the augmented exercise therapy was found on ADL, at least based on the Action Research Arm Test (Kwakkel et al., 2004a). However, the studies included in this meta-analysis were conducted on patients in the post-acute phase of stroke (i.e. within six months after stroke).

The current study has also shown no significant improvement in subject capabilities that would support the use of augmented therapy for upper limb function in a sample of chronic stroke patients evaluated in the three domains of the ICF. Even for digital dexterity, which is highly reduced for the paretic hand, intensive rehabilitation in our study did not improve subject performance levels. Furthermore, most of our patients continued to receive, two or three times a week, additional physiotherapy that was not specific to precision grip. Despite this, the addition of specific grip-lift rhythmic task-oriented auditory cued therapy did not improve grip-lift parameters, dexterity, activity and satisfaction in our chronic stroke patients. On the one hand, the effect on repetitive training of the upper limb remains unclear (French et al., 2010). On the other, the lack of improvement could suggest that the subjects already reached their plateau of recovery or that the therapy was insufficiently constraining. Furthermore, as a result of weariness the patients could hardly increase the number and/or the duration of the training sessions.

Our study has a limitation. Indeed, the inclusion criteria have restricted the number of participants. Each participant had to present manual disability but be able to execute the grip-lift task at inclusion. The limited number of participants could affect the statistical significance of our tests. However, the differences between each evaluation were small and are not clinically relevant. Additionally, the sample size needed to observe a significant modification for the tested parameters was high (at least 87 subjects) suggesting that the therapy didn’t show clinical relevant possible effect. It has to be noted that all patients presented a subcortical lesion that possibly affect interhemispheric connections limiting the transfer of internal models and the disinhibition process (Luft et al., 2004b).

Finally, in contrast to our study, published literature from other countries indicates positive improvements as a result of conventional therapy in chronic stroke subjects (Muellbacher et al., 2002). The current study was conducted in Belgium, and the participating subjects may probably have already reached a recovery plateau as a result of an intensive long-term rehabilitation program since the acute phase after stroke. Presently, considerable differences in the type of rehabilitation care and outcome of different countries have been reported (Brandt, 2007; De Wit et al., 2007). Substantial, knowledge of the therapy given to this category of patients in different countries would provide a more objective means of comparing the resultant capabilities of test subjects in the published literature, as well as identifying combinations of therapies at specific time periods following stroke, which may contribute towards accelerating recovery (French et al., 2010). Hence, if our therapy had been administered during the early phase after stroke, different results may have been obtained, which is worth consideration for future studies.

CHAPTER IV: Development of fMRI evaluation of precision grip

IV.1. Grip-lift forces and EMG measurements throughout a grip-lift task executed during fMRI at 3T

Abstract

This study aims to design an fMRI compatible force transducer capable of measuring safely, simultaneously, and accurately the grip and lift forces under each finger during a grip-lift task and, the related electromyography (EMG) of the First Dorsal Interosseous (FDI) muscle, without compromising the quality of fMRI data. To illustrate our purpose, two volunteers performed a unilateral and bilateral grip-lift task with a mini-block design, each epoch lasting 12.5s for one grip-lift and release. The EMG signal was observed every 2500ms during a 320ms silent period at the end of each repetition time. Unilateral FDI activation or bilateral muscle activity was detected during respectively unilateral or bilateral movements. Comparison of the grip-lift parameters measured before and during fMRI acquisition failed to detect any significant difference indicating that the mathematical treatment of the data acquired during fMRI did not affect the calculated parameters (all $p>0.079$). In parallel no artifact was found in the MR images. The equipment and the experimental design presented in this study allow the simultaneously recording of forces, EMG and fMRI data during a grip-lift task, allowing more comprehensive fMRI experiments examining prehension in healthy or impaired subjects taking into account a maximum of influent parameters.

Submitted as:

Dispa D., Grandin C., Dricot L., Detrembleur C., Penta M., Thonnard JL. Grip-lift forces and EMG measurements throughout a grip-lift task executed during fMRI at 3T.

INTRODUCTION

In order to have a comprehensive understanding of human digital dexterity, a thorough analysis of the precision grip is necessary, together with a description of the corresponding neural correlates.

Collecting both information during the same task represents a technical challenge that few authors were able to achieve. This may be explained by the fact that the practice of, on the one hand, force transducers used to measure the components of the precision grip and, on the other hand, electromyographic (EMG) recordings are hardly compatible with magnetic resonance scanners that are nowadays the main tool used for studying brain activation.

During the precision grip task, the amplitude and time variation of the grip force (GF) perpendicular to the contact surface, and the vertical load force (LF) induced by the object weight and the arm movements, have been well described in healthy subjects (Johansson and Westling 1984). Many studies have also reported how the coordination between GF and LF is disturbed after brain injury (Hermsdorfer et al., 2003; Nowak et al., 2003; McDonnell et al., 2006; Nowak et al., 2007a; Nowak et al., 2007b). However, these data do not allow understanding how the brain is able to precisely adjust GF and LF because the neural networks involved in this task have not been investigated. Moreover, functional magnetic resonance imaging (fMRI) has been used for this purpose but without simultaneous recording of the forces and EMG (Ehrsson et al., 2003; Kawato et al., 2003).

The specific environment of fMRI imposes several constraints upon the experimental design. The strong magnetic field present in the scanner room prevents the use of any ferromagnetic metals that would be attracted to the scanner and induce artifacts in the MR images. Furthermore, the radio frequency and magnetic gradient fields used during scanning, as well as electromagnetic interference may disturb the force measurements and EMG recordings. Inversely, the movements of the arm and/or the head of the subject can disturb the MRI images. Moreover, long EMG and force transducer leads or their movements can also create artifacts in the fMRI data. Finally, conductive loops in contact with the subject must be avoided to prevent burning of the skin.

Some authors have addressed the question of forces and/or EMG acquisition simultaneously with fMRI (van Duinen et al., 2005 and 2007; van

Rootselaar et al., 2007; van der Meer et al., 2010), but only a few describe in details the material and procedures used in their study. Technical studies presenting methods to record and analyze simultaneously forces, EMG and fMRI data are therefore lacking.

The aim of this work was to design a fMRI-compatible force transducer capable of measuring safely, simultaneously and accurately, the grip and lift forces under each finger during a grip-lift task without compromising the quality of the fMRI data. To better mimic physiologic movements, a movable instrumented object was used in contrast with the unmovable devices previously developed. The purpose of EMG recording was to verify muscle activity in one or both hands. Therefore, we voluntarily did not invest in a highly sophisticated method to obtain continuous usable EMG signal but rather focused on intermittent recording. Two subjects were examined to test the procedure. Moreover, one of the subjects illustrates the validation of an fMRI protocol allowing measurement of the grip-lift parameters simultaneously with EMG of the First Dorsal Interosseous (FDI) muscle and brain activity.

METHODS AND RESULTS

Subjects and Tasks

The Biomedical Ethics Committee of the School of Medicine of the Université catholique de Louvain authorized this study. Two healthy right-handed subjects (one male, 28 years old, and one female, 46 years old) gave their written informed consent to participate to this feasibility study. The subjects were blindfolded and lain supine in the scanner with the arms strapped to sides of the chest. This setting allowed limiting the movements to a small displacement of the hand and forearm (the manipulandum being lifted about 5 cm up) and prevented any visual feedback. The manipulandum stood on a wooden support to allow the subject an ease grasp, lift and lowering (Figure IV.1.1). Preliminary tests ensured that neither the manipulandum nor the EMG material induced any overheating during at least 10 min of consecutive echo planar imaging (EPI) recording.

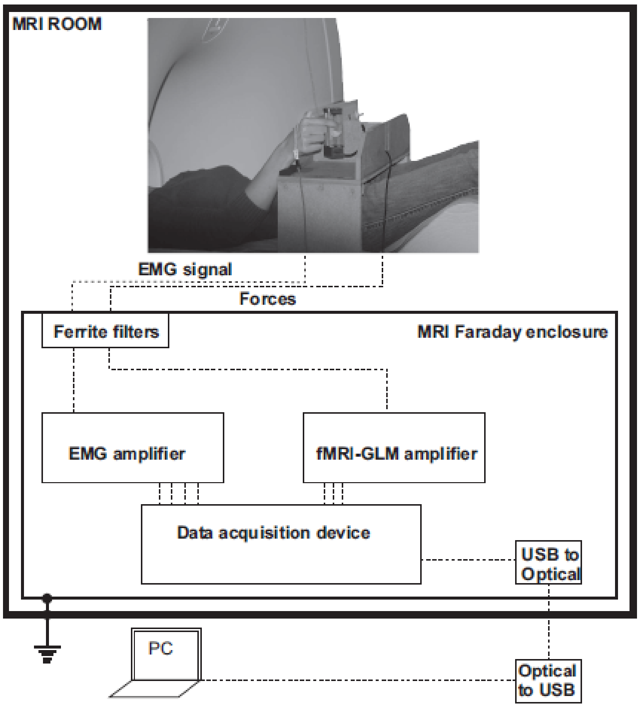

Figure IV.1.1. A picture of a subject in the MRI room with electrodes on the First Dorsal Interosseous (FDI) muscle and the manipulandum in the hand. Wires connected the Faraday enclosure (internal components schematized) inside the MRI room.

To confirm that the manipulandum and the EMG setup did not interfere with the fMRI signal, both subjects executed a block design paradigm consisting, for each run, of 10 grip-lift trials of 12.5 s with a 17.5 s resting period between each trial. One trial consisted of grasping the manipulandum between index finger and thumb, lifting it upwards from the table, holding it stable for several seconds, and finally laying it back on the support and releasing it. Three consecutive runs were performed, each consisting of ten unimanual grasps with the dominant hand. One run was performed with a sham manipulandum (with the same external appearance and weight, but without any sensor), and therefore without any force or EMG recording device in the magnet room, a second run was performed with the whole setup inside of the scanner, followed by a third run with the sham manipulandum. Vocal instructions were given through headphones to tell the subject to be prepared (“right hand”), to start (“go”), and to cease the action (“stop”).

Additionally, the male subject realized a similar block design paradigm. The grip-lift task was then performed either with the dominant right hand or with both hands simultaneously. During the bimanual grip-lift tasks, the right hand lifted the instrumented manipulandum and the left hand lifted the sham manipulandum. The same vocal instructions were given including a bilateral trial announcement ("both hands"). This subject executed two runs of ten trials. In each series, five unimanual and five bimanual trials were randomized. This protocol was first executed outside the scanner room and then repeated during an fMRI session to compare the GF and LF measurements obtained in the two conditions.

The grip-lift manipulandum with forces acquisition

The manipulandum (Arsalis®, fMRI-GLM) was designed to be fMRI-compatible. It was a 275g, 108x56x38mm (height, width, depth) mechanical assembly with two 62x37mm rectangular Plexiglas contact surfaces (Figure IV.2A). The body of the manipulandum was made of titanium to avoid overheating and interference with the MR imaging. The base weight of the manipulandum was 275 g, which could be increased to 500 g by manually replacing the screwed inertial weight. This weight kept the center of gravity of the device at the same location between the grip surfaces.

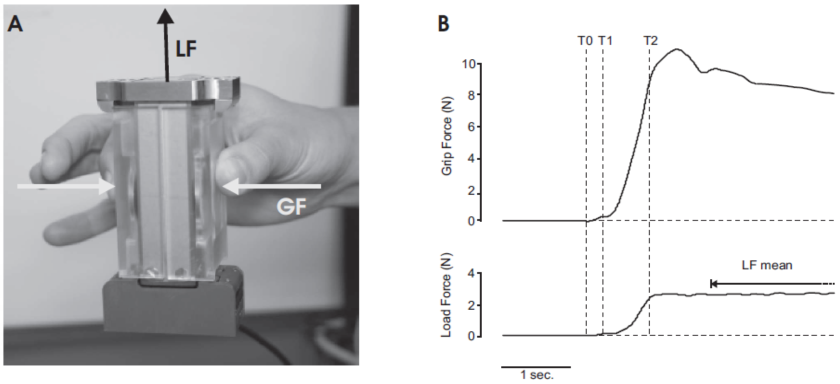

Figure IV.1.2 (A) The manipulandum and vectors illustrating the forces: grip force (GF) in grey and load force (LF) in black. (B) Typical recordings of LF and mean GF exerted by the two fingers. The vertical dotted lines indicate the temporal parameters: T0-T1=preloading phase; T1-T2=loading phase.

The manipulandum was instrumented with full Wheatstone Bridges incorporating three strain gauges allowing the force perpendicular to each contact surface (GF left and GF right), as well as the total tangential force applied on the object (LF), to be measured (Figure IV.1.2A and B). Each sensor used a binocular design with yield strength of 300N. The manipulandum was calibrated up to a full scale of 30N in each direction and demonstrated a maximum nonlinearity of 0.70 and 0.35 percent of full scale for the LF and both GF directions, respectively. The analogue signals were pre-filtered with ferrite beads (Multicomp®MCAB035060-33), amplified, filtered with a Bessel, 4-pole, 150Hz cut-off low-pass filter and then sampled at 2000Hz with a 16-bit resolution. The resolution of the forces measurements was 0.002N for the grip force and 0.001N for the load force. The data were stored on a personal computer for off-line analysis. To allow bimanual grasping and to test the motor task without any recording material, a second manipulandum with the same external appearance and weight, but without any sensor, was also used (sham manipulandum).

The forces were recorded and analyzed during the testing paradigm (only with the male subject). Those recordings were analyzed as previously described by other authors (Johansson and Westling 1984; McDonnell et al. 2006). The mean GF was defined as the average of the right and left GF. The following temporal parameters were computed on the force traces (Figure IV.1.2B): the preloading phase (T0-T1; i.e. the delay between the onset of GF and the onset of LF) and the loading phase (T1-T2; i.e. the delay between the onset of LF and the time when LF is equal to the weight of the manipulandum). One dynamic parameter, LFmean (the mean load force during the steady phase when LF was stable for at least one second), was chosen to verify the similarity of the forces recorded inside and outside of the MRI environment.

The radio frequency (RF) of the fMRI acquisition induced noise on the force signals. Each peak of noise associated with the RF was selected and the force signal during the noise period was replaced by a linear interpolation (50 points at 2000Hz for each peak). After this operation, we filtered the force signals forward and backward with a 4th order low-pass Butterworth filter (4Hz).

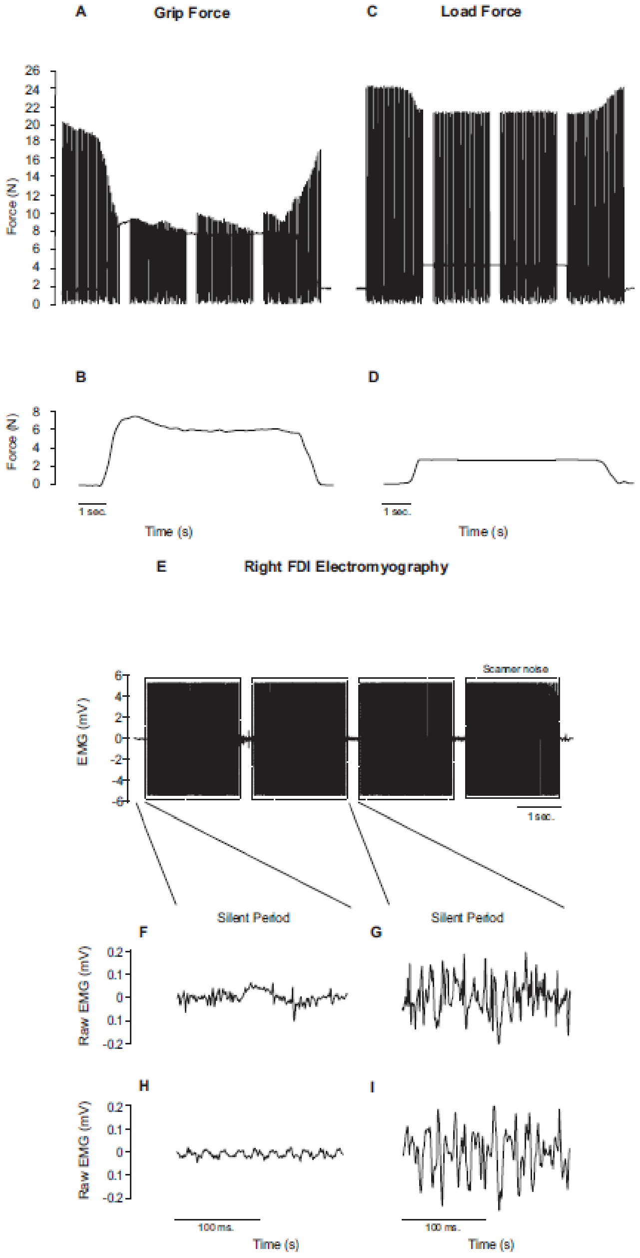

Figure IV.1.3. Grip Force (A,B), Load Force (C,D). A and C: raw traces of the forces. B and D: forces after treatment. First Dorsal Interosseous (FDI) muscle electromyography traces during fMRI acquisition (E,F and G) or outside the MRI room (H,I). F-I: close-up of the EMG raw traces before (F,H) and during (G,I) the grip-lift task.

Figure IV.1.3A and 3C present the raw GF and LF traces for one typical unilateral grip-lift trial executed during an fMRI acquisition. Figure IV.1.3B and 3D show the same traces after noise correction and filtering. Table IV.1.1 presents the median values and interquartile range for the grip-lift parameters measured during ten unilateral grip-lift trials executed either outside the MRI room or during the fMRI acquisition for the male subject. A Mann-Whitney rank sum test compared the grip-lift parameters before and during fMRI acquisition and failed to detect any significant difference, indicating that the mathematical treatment of the data acquired in fMRI did not significantly affect the calculated parameters (all $p>0.079$).

Table IV.1.1: Grip-Lift values of one healthy male subject lying supine outside MRI room and during fMRI acquisition (Mann Whitney rank sum test)

	Outside MRI room (n=10)	**During fMRI (n=10)**	**p-value**
	Median [Range]	Median [Range]	
Unilateral Right hand			
Pre-loading phase (ms)	129.9 [107.2-279.9]	118.5 [57.8-183.1]	0,236
Loading phase (ms)	711 [536.8-915.2]	469 [433.8-739.5]	0,079
Mean LF during stable phase (N)	2.6 [2.5-2.6]	2.6 [2.6-2.6]	0,741
Bilateral (Right hand values)			
Pre-loading phase (ms)	152.8 [83.4-292.1]	121.3 [100-176.2]	0,91
Loading phase (ms)	832.2 [488.5-947.4]	739.2 [707.2-775.7]	0,571
Mean LF during stable phase (N)	2.6 [2.6-2.6]	2.6 [2.6-2.6]	0,515

EMG

The electrical activity of the FDI muscle was measured using surface solid gel silver/silver chloride electrodes (Neuroline®70001-K). These electrodes were placed on both hands after cleaning of the skin with alcohol and ether, one on the belly of the FDI muscle, the other on the second metacarpophalangeal joint. A neutral electrode was placed on the external malleolus. The leads of the electrodes were strapped to the hand's subject so that their movements were limited to the small movements of the forearm during the lift up and lay down of the manipulandum. The raw EMG signals were pre-filtered by ferrite beads (Multicomp® MCAB035060-33), amplified, band-pass filtered (Bessel 2-pole, low frequency cut-off 18Hz, high frequency cut-off 2kHz) and then sampled at 2000Hz with a 16-bit resolution. To prevent conductive loops, the first stage of amplification in the EMG amplifier was battery powered and then optically coupled to the subsequent data processing chain. This provides complete galvanic isolation of the subject relative to data acquisition system.

During fMRI acquisition of the paradigm testing with the male subject, the EMG of the FDI muscle was analyzed during the silent periods occurring every 2500ms for 320ms. A similar method was presented by Liu et al. (2002). This signal was band-pass forward and backward filtered (20-200Hz, Butterworth 4th order) and rectified.

A trained observer visually evaluated the on/off activity of both FDI muscles. This method has been shown to be the easiest and most reliable EMG method (Basmajian 1979; Dierick et al., 2002).

Figure IV.1.3 (E-I) presents the dominant hand FDI EMG activity for one typical trial during fMRI acquisition (E-G) or outside the MRI room (H, I). This figure demonstrates that undisturbed EMG signals could be recorded during the silent period at the end of each TR. The middle panels show the FDI muscle activity during the silent period, when the subject did not touch the object (Figure IV.1.3F), and when the subject held the manipulandum static in the air (Figure IV.1.3G). The lower panels show the EMG activity during a trial acquired outside the MRI room before the grip-lift task (Fig. IV.1.3H) and during the static holding phase (Figure IV.1.3I). The EMG measurements allow us to detect potential mirror contractions of the resting hand. Independent of the condition (inside or outside MRI room), in all unilateral trials, only unilateral right hand contractions were detected without mirror contractions. Similarly, in every bilateral trial, bilateral FDI activation was detected.

The Faraday enclosure

The electronic components that may include ferromagnetic parts were isolated in an aluminum box acting as a Faraday cage (Figure IV.1.2) and located inside the MRI room as far away as possible from the magnet. The cables were plugged into the front panel of the aluminum box and then connected, inside the box, to the amplifiers of the manipulandum and the EMG. Amplified signals were transmitted to a data acquisition device (National Instruments®, NI-DAQ USB-

6221) and then transmitted via an USB-optical cable to a personal computer located outside the room.

MRI

Anatomical and functional images of the entire brain were acquired in the anterior commissure, posterior commissure (AC-PC) orientation (for both subjects) using a 3T scanner equipped with an eight-channel phased-array head coil (Achieva, Philips Healthcare®, Best, The Netherlands). For anatomical images, a 3D fast T1-weighted gradient echo sequence with an inversion prepulse (Turbo Fiels Echo [TFE]) was used with the following parameters: field of view=230x208 mm, slice thickness =1 mm, acquisition matrix=284x217, 150 slices, repetition time (TR)=9 ms; echo time (TE) =4.6 ms; flip angle=8° , SENSE factor (parallel imaging)=1.5.

For functional images, a 2D gradient echo single-shot echo-planar imaging (EPI) sequence encompassing the entire brain was used with the following parameters: 36 slices; slice thickness=3.5 mm, no gap, field of view=230x230 mm; acquisition matrix=92x94; TR=2500 ms; TE=32 ms; flip angle=90° SENSE factor=2.5. The temporal slice timing was set to minimum to group the radio frequency peaks at the beginning of the TR. This created a silent period of 320ms at the end of each TR, during which EMG signals could be recorded without interference. This window of 320ms was sufficient to record the EMG signal and represented the best compromise between the length of the TR and the frequency of EMG recording periods (every 2.2s).Five brain volumes were acquired for each active block, with a total of 50 active brain volumes for each task (unimanual grip-lift trial, bimanual grip-lift trial).

All FMRI data were analyzed using BrainVoyager QX (Version 2.2.1 Brain Innovation, Maastricht, The Netherlands). Prior to statistical analysis, the functional data underwent a series of preprocessing steps, namely slice scan time correction, 3D motion correction (with realignment to the first volume), linear trend removal, and high pass filtering (removing frequencies lower than 3 cycles/session).

For the testing paradigm (male subject only) both anatomical and functional data of the two first runs were transformed into Talairach space (Talairach and Tournoux, 1988).

Subsequently, the functional data were analyzed using multiple regression models (General Linear Model, GLM) consisting of predictors, which corresponded to the particular experimental conditions of each experiment. The predictor time courses used were computed on the basis of a linear model of the relation between neural activity and hemodynamic response (Boynton et al., 1996).

The movement corrections made during the realignment procedure were smaller than 1 mm and 1 degree for the translation and rotation, respectively, and any abnormal artifact was detected by visual inspection of the recorded images, making the data usable. No task-correlated artifact was observed.

Then, the statistical t-maps with the contrast ["right unilateral grip-lift"–rest] were overlaid to the 3D T1-weighted scans at $p<0.001$ (Bonferoni corrected) and a minimal cluster size of 150 voxels for each of the 3 runs of both subjects (the data were kept in the AC-PC plane without deformation). The observed activity is presented in figure IV.1.4.

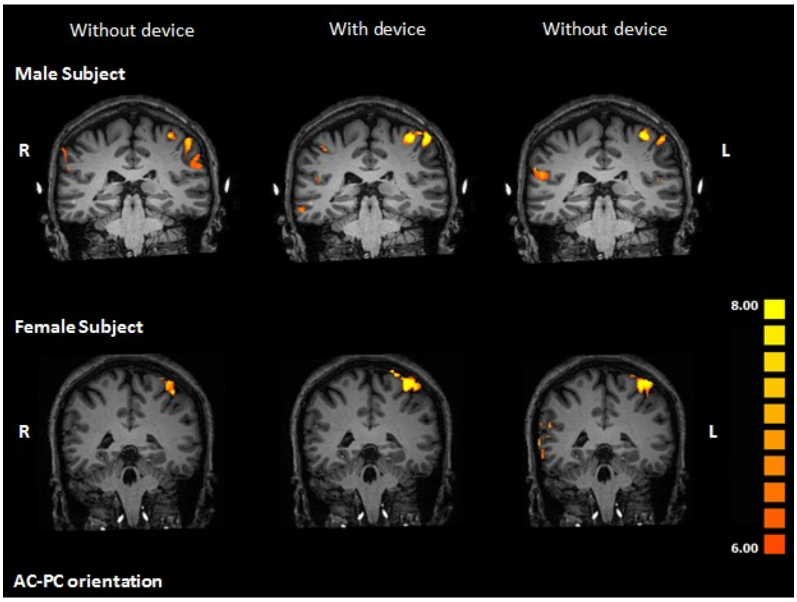

Figure IV.1.4. Contrast of brain activity during active and rest phases ($p<0.001$, Bonferoni corrected) of two healthy adult subjects in a right hand grip-lift task without (first column), with (second column) and again without (third column) the device and acquisition material in the MRI room. The upper panel presents the male subject activations and the lower panel presents the female subject activations in the anterior commissure (AC)- posterior commissure (PC) orientation, 40mm posterior to the AC plane. The t-values scale is presented on the right side of the figure. R: right and L: left.

Figure IV.1.4 presents an illustration of the cortical activity in M1 for the male and the female subject (respectively panel A and panel B) without, with and again without the device and the material in the MRI room.

Thanks to these maps, the distances (in mm) between the same peaks of activations found for comparisons run 1 and run 3 (without devices) were compared with the distances between peaks for comparisons run 2 and 1 and runs 2 and 3 (with–without device). Moreover, the same comparison was also made with the number of voxels common to those regions across the runs. The distances between peaks of activations in the left postcentral and precentral gyrus and in the cerebellum are similar for comparisons between runs without devices than for comparaisons between run with and without devices: $t=0.97$, $p=0.37$. Moreover, the same results were also found with the number of voxels common to those regions across the runs: $t=0.31$, $p=0.77$.

The pooled standard deviations (SD) of the signal of all voxels across the entire time series were also calculated from the data recorded with, and without, the forces and EMG recording equipment in the MRI room (http://www.iupac.org/goldbook/P04758.pdf). If some noise was introduced in the data with the equipment in place, this would induce signal changes in images and translated into a higher SD of the signal across the time series. The pooled SD of the signal for the three runs performed first without, second with, and third again without the presence of the recording setup in the MRI room were similar in the three runs performed with each subject. The difference between those results was smaller than 8%, with the lowest SD value obtained for the measurement made in the presence of the equipment. This indicates that the forces and EMG measuring equipment did not affect the signal in EPI and that the small differences between the pooled SDs are due to intrinsic instabilities in the MR signal, and to small movements of the subject. Figure IV.1.5 presents the distribution of the SD of the voxels signal for both subjects (from 0 to 50, above this level only a few voxels were present in some ranges of SD).

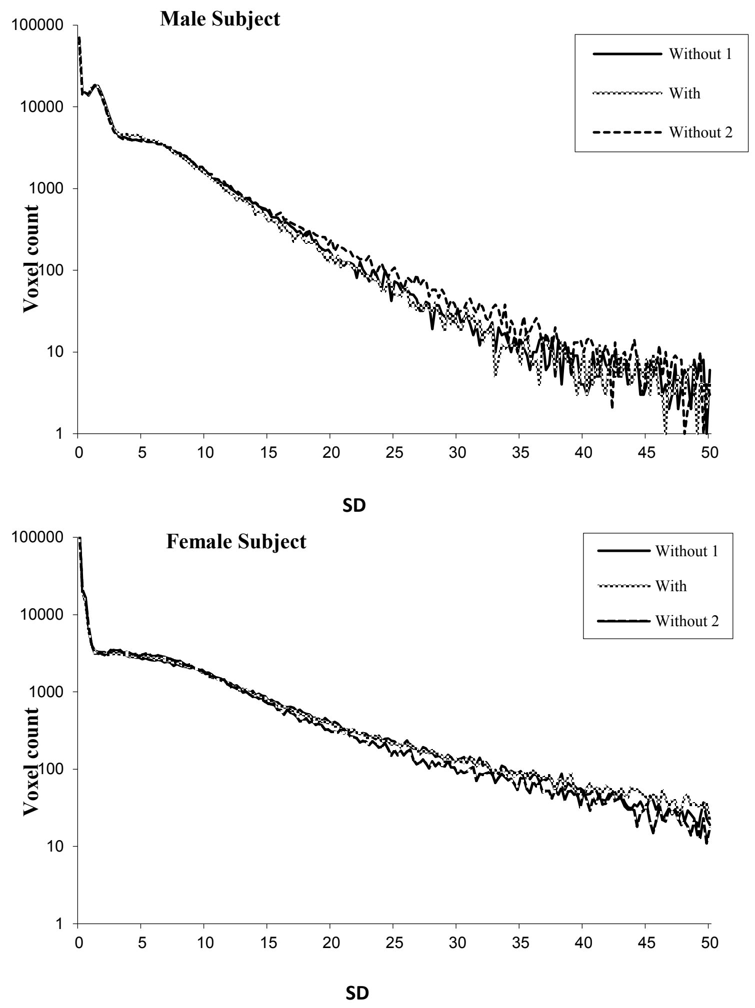

Figure IV.1.5. Distribution of the SD of the signal during fMRI time series represented as the cumulated number of voxels for each range of 0.25 SD without the setup in the MRI room (without 1), with the whole setup in the MRI room (with) and, again without the material (without 2), for 2 subjects.

For the two paradigm testing runs (male subject only), areas activated by the "right unilateral grip-lift" were defined using the contrast ["right unilateral grip-lift" – rest] in the run 1 in conjunction with the contrast ["right unilateral grip-lift" – rest] in the second run. All contiguous voxels with a minimum significance of p<0,05 (Bonferoni corrected) and a minimal cluster size of 150 voxels were selected (t-test). The same statistical t-map was displayed for the bilateral grip lift task. For both tasks, every activated cluster was tabulated with its Talairach coordinates and the corresponding anatomic and Brodmann areas (BA) were defined on the normalized anatomy of the subject by a senior neuroradiologist.

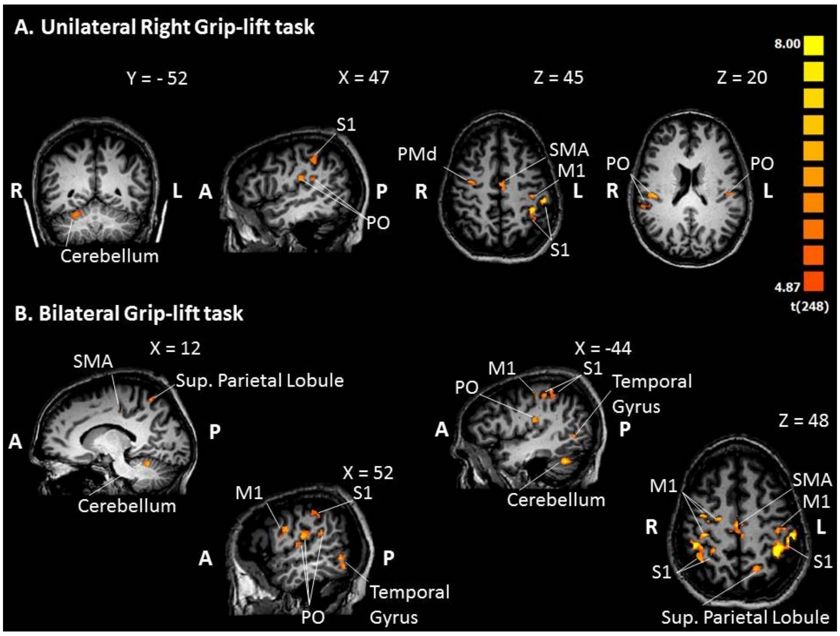

Figure IV.1.6. Contrast of brain activity in one healthy male adult subject during active and rest phases in a right hand grip-lift task (A) and a bilateral grip-lift task (B). The t-values scale is presented on the right side of the figure. A: anterior, P: posterior, R: right, L: left, S1: primary sensorimotor area, M1: primary motor area, SMA: supplementary motor area, PO: parietal operculum.

The right hand grip-lift tasks (Figure IV.1.6 A) significantly activated bilateral primary sensorimotor cortex (postcentral gyrus : S1), the supplementary motor area (medial frontal gyrus: SMA), left dorsal premotor cortex (medial frontal gyrus: PMd), right primary motor cortex (precentral gyrus : M1) and cerebellum while, during the bimanual grip-lift task (Figure IV.1.6 B), we observed bilateral activation of all those areas. For both tasks, some activation was also observed in premotor areas and in the parietal operculum corresponding to the secondary somatosensory cortex (S2) (Table IV.1.2). We can see that the left dominance (number of voxels on the left divided by the number of the left and right voxels) is less pronounced for the bimanual grip-lift task (57% without cerebellum) than for the right hand grip-lift tasks (63% without cerebellum).

Table IV.1.2: Brain activity in the healthy male adult subject during grip-lift task without visual feedback

			mm3	Coordinates (Talairach)		
Brain region	Side	BA		x	y	z
Unilateral right hand grip-lift task						
Precentral gyrus	L	4 or 6	161	-37	-21	50
Medial frontal gyrus (PMd)	R	6	188	32	-8	47
Postcentral gyrus	L	1	821	-36	-38	49
Postcentral gyrus	L	1	293	-49	-29	46
Postcentral gyrus	R	2	174	47	-35	37
Medial frontal gyrus (SMA)	L	6	165	-2	-12	45
Parietal operculum	L	OP3	357	-48	-21	16
Parietal operculum	R	OP1-2-3	359	44	-23	19
Lateral parietal operculum	R	OP3	325	56	-34	22
Cerebellum	R		428	19	-50	-20
Bilateral grip-lift task						
Precentral gyrus	L	4	240	-38	-22	48
Precentral gyrus	R	4	294	31	-9	47
Precentral gyrus	R	4	290	32	-26	48
Precentral gyrus	R	6	282	51	-3	23
Precentral gyrus	R	6	213	19	-12	50
Postcentral gyrus	L	1 or 2 & 40	1911	-40	-35	47
Postcentral gyrus	R	2 & 40	1648	42	-35	43
Postcentral gyrus	R	5	253	24	-41	46
Parietal operculum	L	OP3-4	842	-49	-21	16
Parietal operculum	R	OP3-4	1809	48	-24	18
Lateral parietal operculum	R	OP3	418	57	-33	22
Inter-hemispheric (SMA)	L or R	6	1238	0	-19	45
Superior parietal lobule	L	7	222	-16	-58	49
Superior parietal lobule	R	7	239	14	-55	55
Middle temporal gyrus	L	37	277	-48	-66	3
Middle temporal gyrus	R	37	627	49	-57	-4
Cerebellum, anterior lobe, culmen	L		1922	-17	-53	-20
Cerebellum, anterior lobe, culmen	R		1200	19	-50	-21
Cerebellum	L		464	-43	-53	-24
Cerebellum	L		445	-2	-68	-35
Cerebellum	L		357	-2	-51	-5
Cerebellum	L		150	-30	-42	-42

Regions activated (All p <0.05, Bonnferoni corrected, t=4,87, minimum 150 voxels/cluster) during unilateral and bilateral grip-lift task. L, left; R, right; BA, Brodmann area; x, y, z, coordinates of peak-height voxels (mm).

DISCUSSION

In this study, we designed an experimental setting able to concurrently record fMRI, grip-lift forces and EMG data in order to directly correlate EMG and fingertip forces with the functional cortical network. We demonstrated that good quality grip-lift forces and sparse surface EMG measurements of the FDI muscles of both hands could be acquired during either an unimanual or a bimanual grip-lift task, without compromising the quality of the brain activation maps obtained.

Similarly, we did not observe any difference between the grip-lift parameters recorded outside the MRI room, or during an fMRI acquisition. This confirms that the noise created by the RF peaks did not influence either the timing or the amplitude of the computed forces.

We chose to measure GF and LF with strain gauge transducers, as used by van Duinen et al. (2007), while other researchers have successfully used fibre optics transducers or water pressure in a rubber bulb to obtain artefact free recording (Schmitz et al., 2005; Noble et al., 2011). However, the technical information about those transducers as well as the data processing were not documented in the last cited paper. Our results indicate that after analogue low pass filtering, digital artefact removal and filtering, reliable artefact free force recording can probably also be obtained with strain gauge transducers. Hydraulic pressure transducers were described as another alternative to record the forces simultaneously with fMRI (Liu et al., 2000; Liu et al., 2002; Liu et al., 2004). But in that case, only one force was recorded and this prevents any grip-lift coordination analysis.

The EMG of the FDI muscles was recorded during the silent periods (320ms in duration) that occurred every 2500ms as described by Liu et al. (2000). This restricted time period may be looked upon as a limitation but, in our case, there was no need to record the EMG during the entire fMRI sequence. Indeed, as shown by Dai (2001), the amplitude of the EMG has a low variability in isometric contractions (i.e. during a grip-lift task), allowing to use only certain periods of the EMG. EMG signals permit to verify the bilateral activation time of the FDI muscles during bimanual movements, or to detect mirror movements during unilateral movements. This objective was reached as every bilateral contraction was detected during bilateral grip-lift tasks and inversely unilateral contractions were observed in unilateral tasks. Nevertheless, some authors presented other methods to obtain a continuous EMG trace. Those methods are based on a high sampling frequency and an adapted amplificatory device (van Duinen et al., 2005; van Rootselaar et al., 2007). In that case, the authors aimed to analyze quantitative EMG data which differs from our objectives. Recently, van der Meer et al. (2010) presented another method adapted from electro-encephalography (EEG) recordings in fMRI. This last method needs an EEG amplifier and the use of a specific EEG analysis program.

The designs of the forces and EMG recording systems originated from the safety instructions of the MRI constructor. We were advised to use only optical cables to export signals out of the MRI room in order to avoid any electromagnetic interference. Therefore, the amplifiers were grouped in a small Faraday cage placed inside the MRI room, with one optical cable passing from this box through the wall of the scanner room. This setting contrasts with devices previously developed by Liu et al. (2000; 2002), who used a flat cable passing under the MRI room door to record EMG signals simultaneously with fMRI.

The presence of our equipment in the MRI room during the acquisition did not create any supplementary noise in EPI sequences, as revealed by the pooled standard deviation of the signal calculated with, and without, the recording system. Additionally, the activation maps did not reveal any significant difference in the location of the pre- and post-central foci without and with the material in the fMRI room. Moreover, good quality activation maps revealing the expected sensorimotor network were obtained from the studied male subject.

The grip-lift task proposed in this study disclosed brain activation foci mainly in sensorimotor areas: partially contra-laterally for the unimanual task (ipsi-laterally for the cerebellum), and bilaterally for the bimanual task. The activated areas encompassed M1 and S1, but also included frontal premotor areas and the posterior parietal cortex involved in the motor network, as well as S2. As this study is a feasibility study, only 10 trials of each task (unilateral and bilateral grip-lift) of one subject were presented. Therefore, the fMRI results should be taken as preliminary and require to be confirmed by larger studies in future research.

Our study protocol was designed with the aim of studying disable people. In this perspective, we wanted to use a non-repetitive grip-lift task to correlate forces and EMG data for each trial, allowing us to link the activation pattern with performance, and to exclude wrongly executed trials if necessary.

Nevertheless, our results are similar to those of previous studies of repetitive unilateral precision grip (Ehrsson et al., 2000; Kuhtz-Buschbeck et al., 2008) or repetitive grip-load coupling with the right dominant hand (Ehrsson et al., 2003; Kawato et al., 2003). These authors also reported additional activation in areas such as the cerebellum and the thalamus. The bilaterally increase of activation and the ipsilateral activation observed in the thalamus could be explained by the repetitive nature of the task, which may enhance the neural activity in the sensorimotor network. However, the contribution of small mirror movements cannot be totally excluded, as the EMG was not recorded in these last studies.

Kuhtz-Buschbeck et al. (2001) described the activation obtained with a non-repetitive static precision grip task. In this work, subjects performed grip-lift trials with normal, gentle, or firm grip force during a 30 seconds static phase. In a normal force holding task, only small activations localized in the contralateral central sulcus, intraparietal sulcus and ipsilateral inferior parietal cortex were observed. This limited activation may be explained by the fact that the brain activity was observed only during the 30 seconds static phase, whereas the peak of activation in SMA and M1 is present during the lift-off and the put-down of the object. Indeed, the authors suggested that the dynamic phases of lift and release of the objects are more demanding than static force conditions, which generally evoke less fMRI activity.

To avoid loss of sensitivity in brain activity measurements, we chose to use short trials and we proposed a “mini-block” design, with active epochs of 12.5s. Within this epoch, the time spent to lift off and put-down the manipulandum was about 15%, considering that each dynamic phase lasted about 1 s. We observed consistent activation of the sensory-motor network. This demonstrates that a mini-block trial shorter than a classical block design apparently allows to obtain more brain activation than a longer static grip-lift task (Kuhtz-Buschbeck et al., 2001), while permitting to record simultaneously the forces and EMG signal related to a single trial, which is not possible with a repetitive task.

In conclusion, the equipment and the experimental design presented in this study allow the simultaneously recording of forces, EMG and fMRI data during a grip-lift task. These data may pioneer more comprehensive fMRI experiments examining prehension in healthy or impaired subjects. The simultaneous EMG recordings could be particularly helpful for the evaluation of stroke patients, who often present mirror movements (Daly et al., 2008). In the absence of EMG recording, mirror movements represent a major confounding factor that obscures conclusions made about the reorganization of the motor cortical network in stroke subjects.

Our setup may help in understanding the underlying cortical activation and reorganization involved in precision grip tasks, while taking into account a maximum of influent parameters (forces, muscle activity, grip type). These findings could be used in future research in order to confirm or quantify the impact of rehabilitation therapeutics on the cortical activation of people suffering a variety of precision grip impairments.

IV.2. Effect of position and vision on the grip-lift parameters

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Abstract

The grip-lift task permits a quantitative assessment of grasping ability. Patients are regularly assessed in a supine position, which offers a different view of the grasped object from that in the sitting position. To our knowledge, no data are currently available on the influence of posture and vision on grip-lift task parameters. We therefore aimed to determine the effects of posture and vision on these parameters.

Twenty-six healthy right-handed adults performed grip-lift tasks with a manipulandum that measured different temporal and dynamic parameters in four conditions: sitting eyes open, sitting blindfolded, lying down eyes open and lying down blindfolded.

A repeated measures analysis of variance with two factors (vision and position) revealed that the absence of vision affected all measured parameters. The lying down position increased the time between contact with the object and the first modification of the vertical force as well as the delay between that modification and the start of increase in vertical force. Additionally, there was a lower adaption of the horizontal force, required to squeeze the object, to the vertical force. Finally, the interaction of position and vision was associated with significant differences in the delay between the contact of each digit with the object, the maximum horizontal force and the ratio between the horizontal and vertical force during a static holding period.

Both position and vision appear to affect the grip-lift task. Consequently, sequential assessments should be performed in the same condition in order to obtain reliable data.

This chapter is accepted for publication as:

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INTRODUCTION

The ability to grasp an object can be impaired by several conditions. Grasping ability can be assessed by the grip-lift task, which evaluates the grip force (GF) perpendicular to the contact surface and the load force (LF) parallel to the contact surface that a subject uses to grip and lift an object between the thumb and index finger. McDonnell et al. (2006) highlighted the grip-lift task as a sensitive measure of the loss of fine manipulation after a stroke. Moreover, a good correlation has been reported between grip-lift task parameters and some functional assessment scales. Furthermore, the grip-lift task can be used clinically to quantify deficits in precision grip and the effects of rehabilitation in stroke patients (McDonnell et al., 2009; Nowak et al., 2006). It can also be used in elderly patients to detect increased delays in grasping and lifting objects (Cole et al., 1998) or age-related decreases in grip strength (Nicolay et al., 2005).

The visual and/or kinesthetic information perceived by the subject provides feedback for the prehension task (Oujamaa et al., 2009). However, in the case of an acute injury or due to technical reasons (e.g., functional magnetic resonance imaging evaluation-fMRI), the position of the patient may modify the evaluation of grip-lift task parameters. Richards et al. (1997) reported, in healthy adults, the same maximum grip strength (Jamar dynamometer) in the sitting and lying supine positions with the arm next to the chest and the elbow flexed at 90°. Other authors have discussed the effects of the trunk, shoulder, forearm or wrist position on force production by the upper limb (Kattel et al., 1996; Roman-Liu et al., 2005; Bensmail et al., 2009; Lin et al., 2013). The position of the trunk or the height of the grip with respect to the shoulder influences pull strength (Lin et al., 2013). The maximum voluntary grip strength is apparently modified by the shoulder, elbow and wrist joint angulation (Kattel et al., 1996). Wrist movements during grasping or hyperextension of the wrist joint modified the grip strength and GF during grip-lift tasks (Ambike et al., 2013; Bensmail et al., 2009; McDonnell et al., 2009).

To our knowledge, no study has yet observed the combined effects of position and vision on grip-lift task parameters. The aim of the present study is to determine the influence of position (sitting vs. lying down) and vision (eyes open vs. blindfolded) on grip-lift task parameters in healthy adults. This knowledge may further our understanding of grip-lift tasks in bedridden patients and patients with little or no visual acuity. Moreover, this information may enable comparisons between the grip-lift task performance of bedridden patients and normative data, which have mostly been acquired from subjects performing the grip-lift task in the sitting position (Diermayr et al., 2011; Duque et al., 2003; McDonnell et al., 2006).

MATERIALS AND METHODS

The study protocol was approved by the institutional ethics committee of the Medical School of the Université catholique de Louvain. All participants provided written informed consent.

Subjects

Twenty-six right-handed young healthy volunteers (15women and 11men; mean age, 25.1±1.25years) without any disorders affecting the function of their upper limb participated. The Edinburgh questionnaire determined the percentage of handedness in each subject (Oldfield, 1971; Demura et al., 2006). Participants with limited visual acuity wore their correcting glasses during the evaluation.

Materials and tasks

The subjects sat or lay down on an examination table with a wooden tablet on their legs. Participants were required to grasp a manipulandum between their thumb and index finger (Figure IV.2.1a), lift it, hold it for 6 to 8s and replace it on the tablet. Each subject performed 10 grip-lift trials with the dominant hand, in each of the following four conditions: sitting with eyes open (SO), sitting blindfolded (SB), lying down with eyes open (LO) and lying down blindfolded (LB) (Figure IV.2.1c and d). The order of these conditions was randomly determined, and in every position, one-to-three learning trials were allowed. A sleep mask was used to blindfold the subjects. In the lying down position, the arms were strapped to the chest in order to minimize movements of the shoulder and mimic the position of the arms along the chest in the sitting position. In the LO condition, the subject could at least partially see the manipulandum and certainly see the grip during the lifting of the object (Figure IV.2.1d). For the SO condition, the results of only 25 subjects were recorded because of technical issues in one volunteer.

The manipulandum was equipped with full Wheatstone bridges incorporating three strain gauges to measure the force perpendicular to each contact surface (GFleft and GFright), in addition to the total tangential force applied on the object (LF) (Dispa et al., 2013). Each sensor was of a binocular design with a yield strength of 300N. The manipulandum was calibrated to a maximum scale of 30N in each direction, and demonstrated a maximum nonlinearity of 0.70% and 0.35% of the full scale in the LF and both GF directions, respectively. The analogue signals were amplified and filtered using a four-pole Bessel filter with a low-pass 150Hz cut-off filter and then sampled at 2000Hz at 16-bit resolution. The data were stored for off-line analysis.

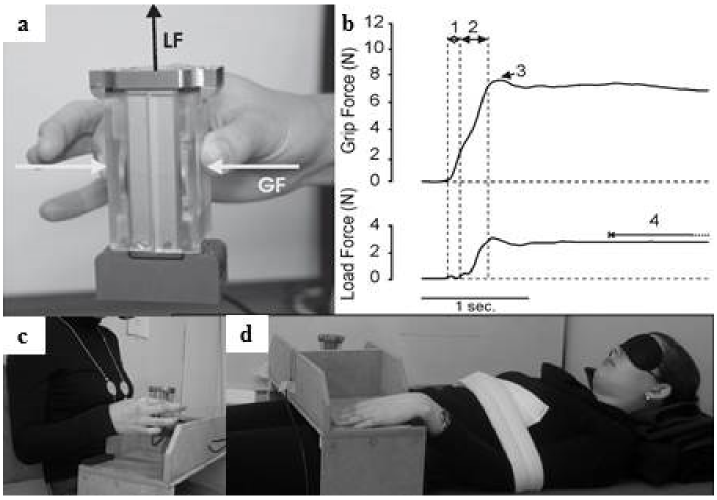

Figure IV.2.1. (a) Manipulandum and vectors illustrating the forces: grip force (GF; gray arrows) and load force (LF; black arrow). (b) Typical recordings of LF and meanGF exerted by the two fingers. The vertical dotted lines indicate the following temporal parameters: 1=preloading phase, 2=loading phase, 3=GF_{max}, 4=stable phase to calculate the hold ratio. (c) Picture of a subject lifting the manipulandum in sitting position. (d) Picture of a subject in lying down position.

The following parameters were measured (Figure IV.2.1b) (McDonnell et al., 2006; Duque et al., 2003): (1) preloading phase, i.e., delay between the onset of the GF and the onset of the LF (threshold, 0.1N), (2) loading phase, i.e., delay during which both GF and LF increased until the LF equaled the weight of the manipulandum (2.75N), (3) GF_{max}, i.e., maximum GF when the object was lifted, and (4) the hold ratio, i.e., meanGF/meanLF during the stable phase, which started a minimum of 1s after GF_{max} was reached and which lasted for at least 2s. Additionally, the delay between the contact of the thumb and index finger with the manipulandum was calculated, as well as the delay between the contact of the first finger with the manipulandum and the onset of LF. Moreover, the following parameters were extracted from the first derivative of GF and LF during the preloading and loading phases: (a) mean GFrate, which was calculated between the onset and the peak of GF (dGF/dt), and (b) peak GFrate. The precise synergy between GF and LF was calculated for each trial by means of a cross-correlation function between dLF/dt and dGF/dt. To determine the larger coefficient of correlation, one signal was shifted with respect to the other in steps of 2.5ms. This method provided two values for each trial: (a) the maximum coefficient of correlation, which indicates the similarity between the profiles of the force rates, and (b) a time-shift, which indicates the asynchrony between dGF/dt and dLF/dt (Duque et al., 2003).

Statistics

To observe the influence of position and vision on grip-lift task parameters, we used two way repeated measures analysis of variance (RM ANOVA). In case of significant difference ($p<0.05$), Holm-Sidak post-hoc analysis was performed to reveal the influence and interaction of each factor.

RESULTS

The absence of vision regardless of the position, the position regardless of vision and the interaction between the two were found to influence grip-lift task parameters (Figure IV.2.2, Tables IV.2.1 and IV.2.2).

When the subject could not see the manipulandum, the time taken to grasp and lift was increased regardless of the position. Indeed, all temporal grip-lift parameters were significantly increased (by 21%–73%) when the subjects were blindfolded, regardless of the position (all p-values<0.001). The absence of vision also significantly increased the GF_{max}, hold ratio and time shift (by 8%–29%, all p-values<0.001). In effect, the coordination of the forces seemed less accurate in absence of vision. In that condition, the cross-correlation coefficient significantly decreased (by 3%, p-value<0.001; Table IV.2.1).

Table IV.2.1. Influence of position and vision on grip-lift task parameters of the dominant hand in healthy adults (n = 26)

	Position			**Vision**		
	Sitting Mean (SD)	**Lying down** Mean (SD)	**p-value**	**Eyes open** Mean (SD)	**Blindfolded** Mean (SD)	**p-value**
Thumb-index delay (ms)	61 (42.6)	60 (24.03)	0.860	44 (19.7)	76 (38.0)	<0.001*
First contact-LFonset (ms)	99 (66.4)	127 (99.5)	0.005*	87 (52.4)	139 (102.7)	<0.001*
Preloading phase (ms)	159 (92.4)	184 (109.1)	0.036*	131 (63.9)	213 (114.8)	<0.001*
Loading phase (ms)	360 (133.8)	373 (122.9)	0.490	331 (121.6)	401 (125.2)	<0.001*
GF_{max} (N)	6.80 (2.79)	6.93 (2.182)	0.697	6.48 (2.395)	7.25 (2.535)	<0.001*
Hold ratio (GF/LF)	1.88 (0.717)	1.94 (0.67)	0.442	1.83 (0.67)	1.98 (0.703)	<0.001*
Time-shift (ms)	59 (40.0)	67 (37.61)	0.017*	55 (35.02)	71 (40.9)	<0.001*
Cross-correlation coefficient	0.89 (0.063)	0.86 (0.077)	<0.001*	0.89 (0.062)	0.87 (0.077)	<0.001*

P values determined using two-way repeated-measures analysis of variance. * = significant (p < 0.05), NS = non-significant.

Subjects took longer to place their fingers on the object as well as to prepare to lift it in lying than in sitting position, regardless of vision. In fact, the delay between the contact of the first finger and LFonset, the preloading phase and the time-shift were significantly higher in lying than in sitting position (by 28%, 16% and 14%, respectively; all p-values<0.036). However, GF_{max} and the hold ratio were not significantly modified by position. The cross-correlation coefficient decreased slightly (by 3%) but significantly in the lying down position, indicating a less accurate coordination between the forces (p-value<0.001; Table IV.2.1).

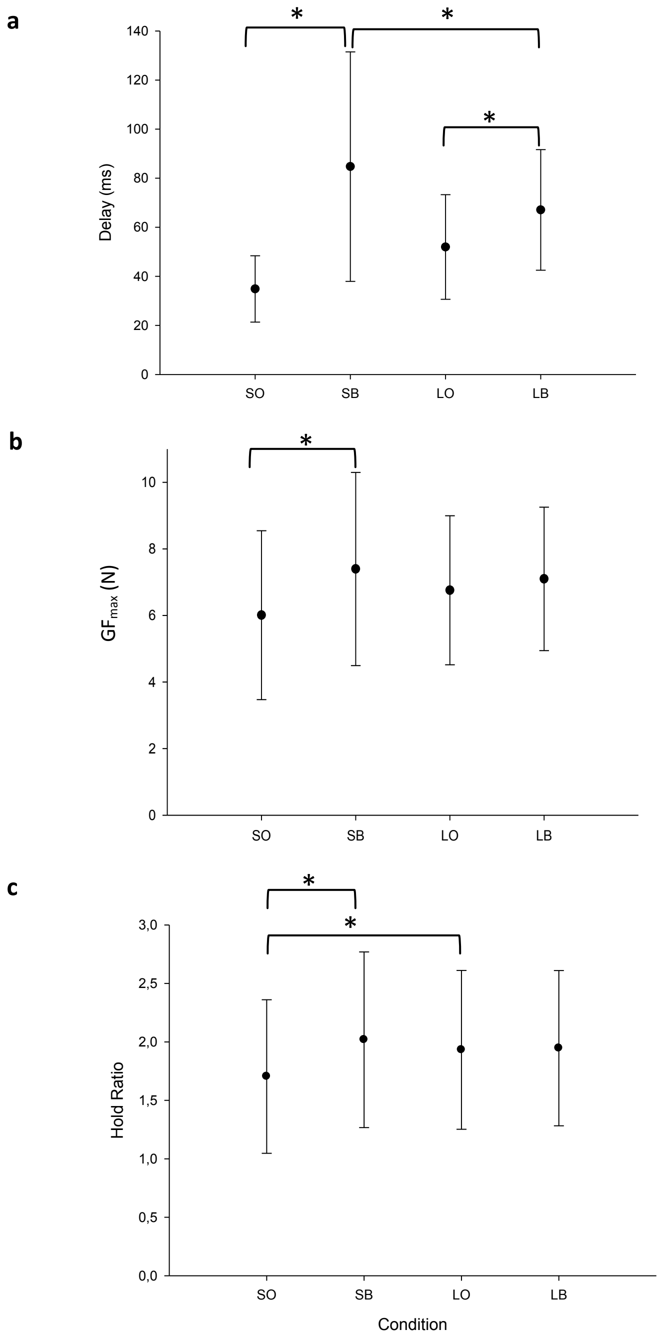

Figure IV.2.2. Scatter plot with error bars of (a) the delay between the contact of the thumb and index finger, (b) the maximum grip force (GF), and (c) the GF hold ratio during the steady phase. SO: sitting position, eyes open; SB: sitting position, blindfolded; LO: lying down position, eyes open; and LB: lying down position, blindfolded. *: statistically significant (all $p < 0.044$).

Two way RM ANOVA revealed significant interactions between position and vision for three parameters: delay between the contact of the thumb and index finger with the manipulandum, GF_{max} and hold ratio (respective p-values=0.003, 0.017 and 0.006; Table IV.2.2). The Holm-Sidak post-hoc test highlighted several significant interactions for these three parameters (Table IV.2.2). In the sitting position, the absence of vision increased the delay in the contact of the thumb and index finger with the manipulandum (post-hoc corrected p-value=0.04). The same augmentation was observed in LB condition (post-hoc corrected p-value<0.001). Additionally, when the subjects were blindfolded, the delay was significantly longer in sitting than in lying position (post-hoc corrected p-value=0.023). For this parameter, the shorter delay and smallest variation were observed in SO condition (Figure IV.2.2a). The interaction between the sitting position and vision significantly increased GF_{max} in SB condition (post-hoc corrected p-value<0.001; Figure IV.2.2b). The hold ratio was significantly increased in the sitting position when the subjects were blindfolded (post-hoc corrected p-value<0.001). Additionally, the last parameter appears to be significantly increased in LO condition as compared to that in SO condition (post-hoc corrected p-value=0.044; Figure IV.2.2c).

Table IV.2.2. Interaction between position and vision in a grip-lift task with the dominant hand in healthy adults (n = 26)

	Sitting		**Lying down**			**Post-hoc (Holm-Sidak)**			
	Open eyes Mean (SD)	Blindfolded Mean (SD)	Open eyes Mean (SD)	Blindfolded Mean (SD)	**p-value**	Sight × Sitting	Sight × Lying	Position × Open	Position × Blindfolded
Thumb-index delay (ms)	36 (13.5)	85 (46.8)	52 (21.3)	67 (24.6)	0.003*	<0.001*	0.040*	NS	0.023*
First contact-LFonset (ms)	75 (46.8)	122 (74.7)	98 (55.9)	155 (123.9)	0.566				
Preloading phase (ms)	112 (55.7)	206 (97.1)	150 (66.3)	219 (131.8)	0.273				
Loading phase (ms)	317 (112)	403 (139.6)	346 (130.1)	399 (111.6)	0.306				
GF_{max} (N)	6.20 (2.537)	7.40 (2.902)	6.76 (2.238)	7.10 (2.16)	0.017*	<0.001*	NS	NS	NS
Hold ratio (GF/LF)	1.74 (0.657)	2.02 (0.751)	1.93 (0.679)	1.95 (0.664)	0.006*	<0.001*	NS	0.044*	NS
Time-shift (ms)	48 (29.2)	69 (46.0)	62 (39.0)	73 (36.1)	0.365				
Cross-correlation coefficient	0.91 (0.050)	0.88 (0.069)	0.87 (0.069)	0.85 (0.085)	0.209				

P-values determined using two-way repeated-measures analysis of variance. * = significant ($p < 0.05$), NS = non-significant. Results of Holm-Sidak tests (post-hoc) are given for parameters with significant two-way repeated-measures analysis of variance p-values.

DISCUSSION

In healthy adults, the loss of vision significantly increases all time related grip-lift task parameters, regardless of the position in which the task is performed. According to the literature, these parameters are modified when the subject is blindfolded, in young and old patients, and in patients with cerebral visual impairment (Cole et al., 1998; Timmis et al., 2012). Tactile feedback is essential for fine manipulation, but contact between an object and the hand involves feedforward and feedback loops that operate through vision and proprioception (Johansson, 2002; Flanagan et al., 2006; Johansson and Flanagan, 2009; Dispa et al., 2013; Mugge et al., 2013; Botzer and Karniel, 2013).

When the subjects were blindfolded, GF_{max} and the hold ratio slightly but significantly increased. In discrete events, sensory-driven control, including visual, proprioceptive and tactile senses, provides feedback and permits the adaptation of the hold ratio. The loading of the object is initiated through a prediction adaptation and then corrected, if needed, due to the sensorimotor feedback (Dispa et al., 2014; Li et al., 2009; Diermayr et al., 2011). In our study, as in cutaneous anesthesia, GF_{max} and the hold ratio were increased owing to the safety margin, which the subject applies to avoid slipping of the object (Augurelle et al., 2003; Johansson, 2002). In the LO position, these two parameters were not significantly modified in comparison to the standard SO position.

It appears that without vision, whatever the position, the correlation coefficient and time-shift were significantly different from the results in the “eyes open” condition (Table IV.2.1). The coordination of GF and LF could be linked to an internal model of the mechanical properties of the object. This model is constructed on the basis of the subject’s experience, permitting to anticipate the effects of movement on the object and arm accelerations (Duque et al., 2003; Augurelle et al., 2003). Our data corroborate that visual information provides feedback to adjust these movements. Indeed, in the absence of vision, all grip-lift task parameters were modified.

Regardless of vision, the delay between the first contact with the manipulandum and LFonset as well as the preloading phase and time-shift were higher in the lying down position than in the sitting position. In addition, the cross-correlation coefficient was decreased, suggesting a less accurate coordination of the

GF and LF. Kawato et al. (2003) demonstrated that the feed-forward model permits the control of the hand and arm trajectory. In the present study, when the subjects lay down, the feedforward model could have been less adjusted because of the little experience that the patients had of performing such a task. Moreover, from a mechanical point of view, the position of the elbow differs between the sitting and lying down positions. Almost three decades ago, Mathiowetz et al. (1985a) reported that maximum voluntary isometric grip and key pinch strength were higher with the elbow flexed at 90° than with a fully extended elbow. In fact, the slightly lengthened elbow flexor muscles in the lying down position imply that the position of the sarcomere filaments is probably not optimal. Rassier et al. (1999) confirmed this length-force couple in isometric contractions but not in concentric contractions, such as the one used in our study. Kasprisin et al. (2000) showed in a study utilizing electrophysiology, the influence of the elbow flexion in the activation threshold of the biceps brachialis muscle during a maximal voluntary isokinetic contraction. This information indicates that in an extended arm, the muscles probably need a higher activation signal to provide the same strength. Some authors have observed a strong influence of wrist position on the GF_{max} between the index finger and thumb (Ambike et al., 2013; Bensmail et al., 2009; McDonnell et al., 2009). Since the wrist position was not modified by the postures in our study design, the absence of a significant difference in GF_{max} between different body positions seems quite obvious.

To our knowledge, no study has investigated the effect of posture on grip-lift task parameters. Richards et al. (1997) observed no significant difference in maximal grip strength using the JAMAR dynamometer following a standardized task performed in the sitting and lying down positions (Mathiowetz et al. 1985b). On the basis of these data, no significant modification of the GF/LF and GF_{max} was expected in the present study. Our findings also confirm that regardless of vision, the cross-correlation coefficient is decreased in the lying down position compared to the sitting position. The time-shift of 67ms in the lying down position is close to the delay described in a feedback situation in a previous study (Kawato et al. 2003). The lack of experience in the lying down position probably limits the involvement of the feedforward model. A training period could permit the adaptation of the feedforward model in this position.

The interaction between vision and posture involved thumb-index delay, GF_{max} and hold ratio modifications. The last two parameters have been reported to be adapted by the subject on the basis of previous experience in order to avoid slipping of the object (Westling and Johansson, 1984; Johansson and Westling, 1984; Johansson, 2002; Flanagan et al., 2006; Cole et al., 1999). However, in the case of uncommon objects, one-to-three grip-lift trials are clearly needed to establish a stable and efficient GF (Westling and Johansson, 1984; Johansson, 2002; Bensmail et al., 2009; Li et al., 2009). Further similar manipulations seem to be necessary to adapt the feedforward model to unusual situations in the lying down position (Johansson and Flanagan, 2009).

The short time-shift observed in the SO condition strengthens the hypothesis that successful object manipulation requires the predictive mechanism of the central nervous system oriented by visual information integration before the grip-lift task, based on earlier experiences (Flanagan et al., 2006).

Finally, the hold ratio significantly increases from SO to LO condition as well as from SB to SO condition. These findings are probably the result of the lesser visual perception of the manipulandum in the lying down position, even with the eyes open, than in the sitting position.

In conclusion, our data indicate that regardless of the position of the subject, the absence of vision modifies all grip-lift task parameters. Vision appears essential to the feedforward and feedback mechanisms of the task. Regardless of vision, in the case of dynamic parameters, no significant differences were detected in the lying down position. Some temporal parameters seem to be influenced by position, regardless of vision. For instance, the delay between the contact with the manipulandum and LFonset, preloading phase and time-shift were increased in the lying down position. In contrast, the cross-correlation coefficient appeared to be decreased in that position.

The findings of our study may have clinical implications. In accordance with Mc Donnell et al. (2006) and Nowak (2006), the present study highlights the grip-lift task as a sensitive measure of thumb-index prehension. Consequently, it proves that it is crucial that the task parameters be measured under the same vision and position conditions in order to enable accurate comparisons of the results of multiple evaluations of a subject’s performance.

Further research should focus on the evolution of the grip-lift task parameters during training in different conditions. This knowledge may contribute to the construction of an efficient feedforward model.

CHAPTER V: General conclusion and perspectives

After a general introduction, the second chapter of this thesis reports chronic stroke subjects' deficits in the grip-lift task, particularly regarding predictive regulation and reactive control (Dispa et al., 2014). In the first situation, the chronic stroke patients displayed longer delays with their paretic hand compared with their non-paretic hand and control subjects. Additionally, the paretic hand of chronic stroke subjects had a greater number of slips than did control subjects. Under reactive conditions, the delay after the impact was longer in the paretic hand of chronic stroke patients than in control subjects. In both conditions, the non-paretic hand exhibited non-significant differences in all parameters compared with control subjects. The observed disorders could be due in part to muscular modifications and to an inability to reproduce a motor plan or create one. The latter problem is probably responsible for the greater number of slips.

In the third chapter, we present a repetitive rhythmic rehabilitation for the grip-lift task in chronic stroke subjects (Dispa et al., 2013). Before the therapy, we observed a significant difference in digital dexterity (Purdue Pegboard Test) and the time taken to lift the manipulandum in the paretic hand compared with the non-paretic hand or the dominant hand of control subjects. The correlation of forces also differed between the paretic hand and control subjects. Specific rhythmic bilateral grip-lift task rehabilitation was performed at a frequency of three sessions of 1 hour's duration each week for 8 weeks complementary to the subjects' regular treatment. This training did not improve significantly any of the evaluated parameters. The subjects described greater fluency in the movement and felt that it was easier to perform, but these perceptions were not associated with changes in grip-lift task parameters, digital dexterity, manual ability or satisfaction with and participation in ADL.

Combining the results described in these two chapters of the thesis, it is obvious that chronic stroke patients have grip-lift task and manipulation impairments, and the rehabilitation of these impairments remains challenging.

In chronic stroke patients, the cortical processes of programming and correcting movements are perturbed. During the manipulation of objects in daily life, people are often exposed to dual task situations. Their mind may be occupied by a cognitive task during manipulation; for example, having a discussion while lifting a cup of tea. Guillery et al. (2013) reported the effect of performing a cognitive task concurrently with a grip-lift task in healthy adults. When the subjects were involved in a cognitive task, the time required to take and lift the object (preloading phase) as well as GFmax and GF during the static holding phase were increased. This modification of GF could be linked to anticipation of interference from the concurrent cognitive task, leading to an increase in the safety margin and thereby reducing the risk of the object slipping. Bearing this in mind and considering the modifications of anticipatory processes displayed by chronic stroke patients (see chapter II; Dispa et al., 2014), it would be interesting to observe whether there is an increase in the number of slips or greater grip-lift parameters modifications in these patients compared with healthy subjects. Furthermore, the sensations of ease and fluency described by the chronic stoke patients in the grip-lift rehabilitation programme (see chapter III; Dispa et al., 2013) could be due to a lower cognitive weight of the grip-lift task after training. As suggested by Swinnen and Wenderoth (2004), understanding the link between cognition and action could narrow the gap between behaviour and the neurosciences. Some authors have discussed including dual tasks in rehabilitation programmes to improve walking parameters and cognitive performance in stroke patients (Yang et al., 2007; Kim et al., 2014). Pohl et al. (2011) described the effect of performing a dual task hand movement while walking or speaking. The chronic stroke patients in this study made rhythmical sounds with a small hand clicker or music shaker with either the paretic or the non-paretic hand while walking or speaking. Their walking rate was decreased by concurrently moving the object with the paretic hand. By contrast, their speech rate was increased by moving either hand. The authors concluded that further research is needed employing more functional or ecological exercises and that the impact of dual tasks in rehabilitation must be observed. These suggestions could help to further improve grip-lift task rehabilitation programmes.

The use of ADL and common objects could also provide interesting adaptations of the therapy presented in this thesis. Van Peppen et al. (2012) reported the potential effect of task oriented therapy restricted mainly to a directly trained task, while some authors have discussed the transfer of a specific rehabilitation task to ADL (Summers et al., 2007). Various authors have shown improvements in the time to taken complete tested movements with an impaired upper limb after bilateral treatment (Mudie and Mathias, 2000; Summers et al., 2007). Mudie and Mathias (2000) reported that these improvements were specific to the trained exercise. Summers et al. (2007) observed small changes in impaired limb movement time during the functional evaluation of individuals engaged in unilateral training. The authors concluded that these results demonstrate a generalization from the training of a specific movement to overall upper limb function (Summers et al., 2007). Summers et al. (2007) recommended further studies to determine the most important component of bilateral therapy and to determine which types of patient, with respect to the side and the site of the lesion, could benefit most from bilateral training.

The initial severity of the motor or function impairment appears to be the most important predictors of motor recovery after stroke (Coupar et al., 2012). Some somatosensory parameters seem also to predict upper limb motor recovery, restrictions in activity and participation in ADL (Meyer et al., 2014). These two factors may be correlated to different degrees with two point discrimination, somatosensory evoked potentials, proprioception and light touch. However, such results have been obtained with heterogeneous populations and need to be confirmed. Hamzei et al. (2006) evaluated the effect of CIMT in chronic stroke patients and described two different functional rehabilitation patterns in terms of the level of lesion of M1 and of motor evoked potentials (MEP) in the paretic hand. The authors concluded that larger studies are needed to explore the selection of patients in terms of function by prior fMRI evaluation. Kwakkel et al. (2004b) noted the importance of the first 6 months after stroke onset in at least partially predicting the functional recovery of patients. These authors also recommended further studies to elucidate the impact of task dependent cortical activation patterns through longitudinal studies of functional outcomes. The question of what is kinematically learned during the acquisition of new skills should also be addressed.

Following this last suggestion, the third chapter of the thesis presents a way to add observations of the cortical activations related to a task to its functional evaluation. A fMRI compatible setup permitting evaluation of unimanual and bimanual grip-lift tasks in parallel with EMG, as well as the effect on grip-lift parameters of the subject’s position and view of the object during fMRI, are presented in the first and second sections, respectively, of chapter IV. A fMRI compatible setup and a specific grip-lift task evaluation protocol are described. Moreover, in the second section of that chapter, the position and view restrictions of fMRI are discussed. The lack of a view of the object modified all grip-lift parameters whatever the position of the subject. Regardless of whether the subject could see the manipulandum, the supine position affected the preloading phase, the delay between the contact of the first finger and the onset of LF, the cross-correlation and the time shift. Finally, the interaction of the two parameters (view and position) affected the delay between the contact of the thumb and the index finger, as well as GFmax and the hold ratio.

The possibility of acquiring data on grip-lift parameters and forces concurrently with the activity of the first dorsal interosseous muscle opens the way to new evaluation protocols. It would certainly provide information on cortical activity related to the grip-lift task in impaired subjects. Various authors have already explored this field even without the acquisition of force data and/or EMG recordings. However, though increasing numbers of studies are focussing on fMRI evaluation, some authors suggest caution. Pinter et al. (2013) reported, in seven patients with subacute to chronic stroke, normalization of the ipsilesional primary sensorimotor cortex and SMA while active movements of the affected hand were performed under fMRI after 3 weeks of robotic finger-hand rehabilitation training in addition to conventional therapy. However, no increase in cortical activity was observed in the regions of interest after rehabilitation. Additionally, there was no behavioural improvement. The authors concluded that fMRI evaluation should be used in homogeneous samples. In a meta-analysis of motor-related neural activity after stroke, however, other authors (Rehme et al., 2012) reported that increased activation in contralesional M1 and bilateral premotor areas was highly consistent across different impairment levels and times post-stroke.

The combined techniques of TMS and MRI enabled the observation, in 12 stroke subjects with persistent motor deficits, that individual motor performance depended on corticospinal tract damage, motor cortex excitability and interhemispheric excitability (Volz et al., 2014). The authors concluded that the combination of these three factors accounted for more than 80% of the variance in functional impairment. In another study (Millot et al., 2014), the effectiveness of a therapy was linked to the level of corticospinal excitability. After 8 weeks of robotic exoskeletal arm rehabilitation in chronic stroke patients, there was a greater improvement of manual dexterity as evaluated by the Box and Blocks Test in cases with lower baseline MEP amplitude on TMS.

To summarize these studies, there is a clear interest in using neuroimaging techniques to evaluate subjects' cortical activity and observe rehabilitation-related modifications. However, there is a need for caution in reporting fMRI results without a well selected sample of subjects. In a review of noninvasive cortical exploration techniques, Eliassen et al. (2008) explained that the interest in fMRI is due to it being noninvasive and quantifiable, having high spatial resolution, and allowing multiple acquisition sessions that can be used to follow the patient's progression as a function of time or treatment. These authors also discussed the limitations of this method, suggesting that at least one complementary brain mapping technique should be combined with fMRI. Other authors have evaluated the effect of therapy in chronic stroke patients using two cortical activity exploration methods (Hamzei et al., 2006, 2008; Rijntjes et al., 2011; Könönen et al., 2012). However, precisely the same conditions as during the therapy should be used during fMRI (Eliassen et al., 2008). Considering this last point together with the results of the study presented in the second section of chapter IV of this thesis, attention should be paid to the subject's position and restricted view during fMRI, which could influence motor performance and thereby cortical activity.

To summarize, for further studies, we would suggest realising large multicentric collaborations to evaluate and improve the paretic hand function of a great chronic stroke patients panel. A complete evaluation of the hand function following the three domains of the ICF should include fMRI and TMS evaluations to help the understanding of the effects of the therapy and the categorisation of the patients. The therapy should include functional tasks together with cognitive tasks. The duration of therapy should be at least 60 hours and a cross-over study could highlight the effects of short term intensive treatment (for example 6 hours/ day during 10 days) compared to a less intensive long term rehabilitation (i.e. 1 hour/day, 3 days/week during 20 weeks).

We conclude this thesis with three major points. First, it is clear that there is a need for effective rehabilitation of manipulation in chronic stroke patients. Second, rehabilitation programmes should be related to functional ADL and take into account the cognitive weight of dual tasks. Finally, various adjunctive therapies and evaluation techniques should be developed. Those would both enhance therapy and improve the evaluation and efficacy of treatment for each individual patient.

APPENDIX A: Cortical activity related to the grip-lift task during bilateral precision grip training in chronic stroke patient: a triple case report.

INTRODUCTION

As suggested previously in this thesis, fMRI measures seem to help the comprehension of the cortical activity modifications related to rehabilitation of chronic stroke subjects. A reliable method to evaluate grip-lift task conjoined to fMRI was presented in the chapter discussing healthy adult testing (Chapter IV, section 1). This method including EMG and forces measurements permits to confirm a good understanding and realization of the task, without mirror movements in unilateral trials and with both hands activity during bimanual tasks.

This study aims to complete the evaluation of chronic stroke subjects across multiple testing periods before, during and after 8 weeks of bilateral rhythmic auditory cued precision grip oriented rehabilitation. We combined, on the one hand, the suggestions made in chapter III concerning the cortical activity measures coupled to a functional testing to complement the assessment of chronic stroke patients evolution and, on the other, the use of the complete fMRI compatible grip-lift task setup presented in chapter IV, section 1.

Other authors have shown cortical activity modifications related to either bilateral therapy (BATRAC) or unilateral dose matched rehabilitation (Whitall et al., 2011). The latter study, chronic stroke subjects presented improvements in motor function whatever the realized training. These results seem correlated to an increased cortical activity.

We suggested that in the patients presented in chapter III, who did not improve dexterity, manual ability or grip-lift task parameters, the subjective fluentness and easiness expressed after therapy could be related to early cortical activity modifications.

METHODS

Subjects

The Biomedical Ethics Committee of the School of Medicine of the Université catholique de Louvain authorized this study. Three hemiparetic adults gave their informed written consent.

The subjects were included at least six months after a stroke, which was confirmed by MRI. All patients had completed a neurological clinical evaluation proving hemiparesis by means of the Stroke Impairment Assessment Set (SIAS) (Liu et al., 2002; Chino et al., 1996). The subjects had to be able to lift and hold an object of 250gr between the thumb and index finger during a few seconds. A mini-mental state evaluation (MMSE) was also conducted. The subjects had to score above 26/30, which implied a capability to understand the injunctions and respond to self-reported questionnaires. Patients with other upper-limb pathologies were excluded. A brief description of the subjects is made in table 1 and an illustration of the lesions is presented in figure 1.

Table 1. Pre-study (t0) evaluation results for the 3 chronic stroke subjects

	Age (years)	Sex	Hemiparetic side	MMSE /30	SIAS /76	Lesion description (MRI)	Time since stroke (months)
Patient 1	67	M	Left	26	60	Right fronto-parieto-temporal deep sylvian stroke	6
Patient 2	81	F	Right	29	67	Left lenticulo-striated stroke	12
Patient 3	58	M	Right	28	75	Left capsulo-thalamic stroke	8

MMSE = mini-mental state evaluation; SIAS = stroke impairment assessment set; MRI = magnetic resonance imaging; M = male; F = female

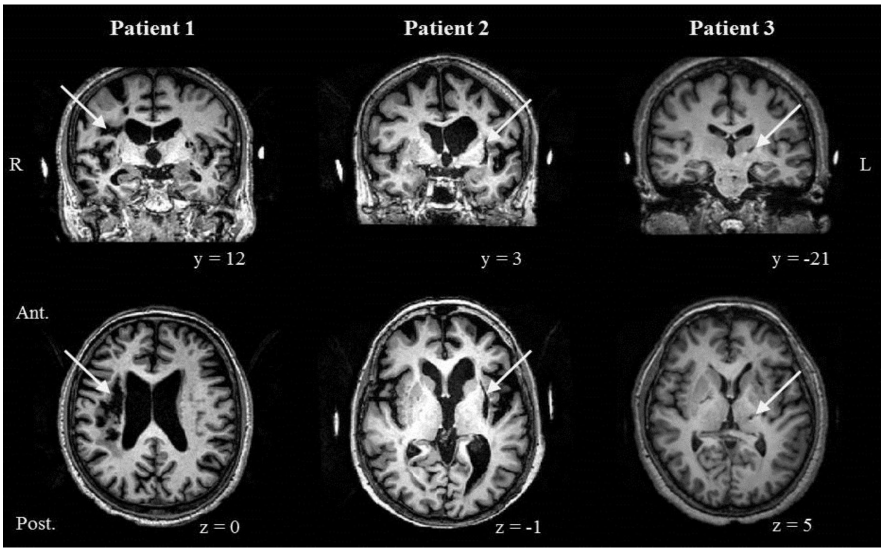

Figure 1. Anatomical images in anterior commissure (AC) - posterior commissure (PC) orientation of three hemiparetic chronic stroke subjects. The first row presents the coronal view and the second row, the transversal view. A white arrow designs the lesion in each view. Ant: anterior, Post: posterior, R: right, L: left. y and z = coordinates are presented as the distance in mm from the AC-PC plane, positive (negative) values are posterior (anterior) and caudal (cranial) compared with the AC-PC plane.

Rehabiliation

The subjects participated to a bilateral rhythmic auditory cued precision grip training during 8 weeks. Three sessions of approximately one hour took place each week. Details of the therapy and exercises are provided in chapter III (Dispa et al., 2013). Prior to the rehabilitation, a delay of four weeks was introduced in order to observe the reproducibility of the evaluations and the supposed plateau phase reached by the patients.

Evaluations

During the twelve weeks program, an evaluation was performed every 4 weeks (t0, t1, t2 and t3). An independent evaluator, blinded to the treatment allocation, assessed the upper limb of the subjects starting with the non-paretic hand.

The manual dexterity was evaluated with the Box and Blocks test (Tiffin and Asher, 1948). The subjects had to move a maximum number of blocks from one side to the other side of a two compartmented box in one minute. The Purdue

Pegboard test permits to quantify the digital dexterity (see chapter III) (Desrosiers et al., 1995). Additionally, the Abilhand questionnaire allows observing the activity limitation of the manual ability in ADL (Penta et al., 2001).

A manipulandum was used to evaluate the patient performance in the grip-lift task before and during fMRI. The complete manipulandum and EMG testing setup is described in Chapter IV section 1. The grip-lift task was realized in a sitting position in the lab, but also in a lying position and blindfolded in the scanner with the arms strapped to the chest. Prior to every fMRI session, the grip-lift was trained in both supine lying and blindfolded condition in the lab to ensure the good understanding of the procedure.

A block design paradigm consisting of ten grip-lift trials of 12.5 s each with 17.5 s of rest between each trial was recorded for each run. One trial consisted of grasping the manipulandum between index finger and thumb, lifting it from the table, holding it stable for several seconds, and finally laying it back on the support and releasing it. Each patient performed 4 runs, starting with the manipulandum in the non-paretic hand and with a sham manipulandum in the paretic hand. The subject performed 2 runs with the apparatus in each hand. In each series, five unimanual and five bimanual grip-lift tasks were randomized. Vocal instructions were given through headphones in order to inform the participant to be prepared (“right hand”, “left hand” or “both hands”), to start (“go”), and to cease the action (“stop”). In this study, focusing on the paretic hand, only the two last runs of each session with the manipulandum in the paretic hand were analyzed (i.e. run 3 and 4).

MRI

Anatomical and functional images of the entire brain were acquired in the anterior commissure (AC)-posterior commissure (PC) orientation (for the three patients) using a 3T scanner equipped with an eight-channel phased-array head coil (Achieva, Philips Healthcare®, Best, The Netherlands).

A 3D fast T1-weighted gradient echo sequence with an inversion prepulse (Turbo Fiels Echo [TFE]) was used with the following parameters: field of view=230x208 mm, slice thickness =1 mm, acquisition matrix=284x217, 150 slices, repetition time (TR)=9 ms; echo time (TE) =4.6 ms; flip angle=8° , SENSE factor (parallel imaging)=1.5.

For functional images, a 2D gradient echo single-shot echo-planar imaging (EPI) sequence encompassing the entire brain was used with the following parameters: 36 slices; slice thickness=3.5 mm, no gap, field of view=230x230 mm; acquisition matrix=92x94; TR=2500 ms; TE=32 ms; flip angle=90° SENSE factor=2.5. The temporal slice timing was set to minimum in order to group the radio frequency peaks at the beginning of the TR. This created a silent period of 320ms at the end of each TR, during which EMG signals could be recorded without interference. This window of 320ms was sufficient to record the EMG signal and represented probably the best compromise between the length of the TR and the frequency of EMG recording periods (every 2.2s) (Chapter IV section 1). Five brain volumes were acquired for each active block, with a total of 50 active brain volumes for each task (unimanual or bimanual grip-lift trials).

All FMRI data were analyzed using BrainVoyager QX (Version 2.2.1 Brain Innovation, Maastricht, The Netherlands). Prior to statistical analysis, the functional data underwent a series of preprocessing steps, namely slice scan time correction, 3D motion correction (with realignment to the first volume), linear trend removal, and high pass filtering (removing frequencies lower than 3 cycles/session). The movement corrections made during the realignment procedure were smaller than 1 mm and 1 degree for the translation and rotation, respectively, and no abnormal artifact was detected by visual inspection of the recorded images, rendering the data usable. We did not observe any task-correlated artifact. For the lesion description the anatomical images were kept in the AC-PC orientation. Concerning the grip-lift paradigm description, both anatomical and functional data were transformed into Talairach space (Talairach and Tournoux, 1988). Co-registrations between functional runs and 3D-T1 weighted scans of each patient were performed automatically, and possibly corrected manually when careful visual inspection identified imperfect co-registration.

Subsequently, the functional data were analyzed using multiple regression models (General Linear Model, GLM) consisting of predictors, which corresponded to the particular experimental conditions of each experiment. The utilized predictor time courses were computed on the basis of a linear model of the relation between neural activity and hemodynamic response (Boynton, Engel et al. 1996).

Areas activated by the “paretic hand grip-lift” before treatment were defined using the contrast [“unilateral paretic hand grip-lift” – rest] in the run 3 and 4 of the first evaluation (t0) in conjunction with the contrast [“unilateral paretic hand grip-lift” – rest] in the 2 last runs of the second evaluation (t1). The same contrast was implemented for the “unilateral paretic hand grip-lift” after treatment considering the 2 last runs of the third and the fourth evaluation (respectively t2 and t3). Additionally, those conjunctions before and after rehabilitation were also realized for the [“bilateral grip-lift” – rest] contrast. All contiguous voxels with a minimum significance of $p < 0,05$ (Bonferoni corrected) and a minimal cluster size of 50 voxels were selected (t-test). The same statistical t-maps were displayed for the bilateral grip lift task. All the maps were overlaid to the 3D-T1 weighted images.

To complete those analyses, a subtraction of the activations observed before and after treatment for unilateral paretic hand movements, as well as bimanual trials, was calculated. All contiguous voxels with a minimum significance of $p < 0,05$ (Bonferoni corrected) and a minimal cluster size of 15 voxels were selected (t-test). The clusters are described for each subject and each condition in tables.

RESULTS

Evaluation of the upper-limb function

The patients didn’t present any significant modification of the digital dexterity, the manual dexterity performance, the manual ability in ADL or the grip-lift task parameters (Chapter III). In contrast, the subjects described fluentness and easiness in precision grip tasks after a few weeks of rehabilitation.

There was a trend toward a slight increase in digital dexterity in some patients across the consecutive evaluations (figure 2), but this did not appear as clinically significant. Patient 3 seemed the most performant and patient 1 increased his mean performance of 1.33 pegs in 30 seconds. Patient 2 presented an increase of 1 peg at t2 but this improvement was not maintained at t3. This could be related either to fatigue, or to a lower implication of the patient at the end of the therapy.

The manual dexterity increased slightly for patient 1 (figure 3). Patient 3 appeared to realize the best performance.

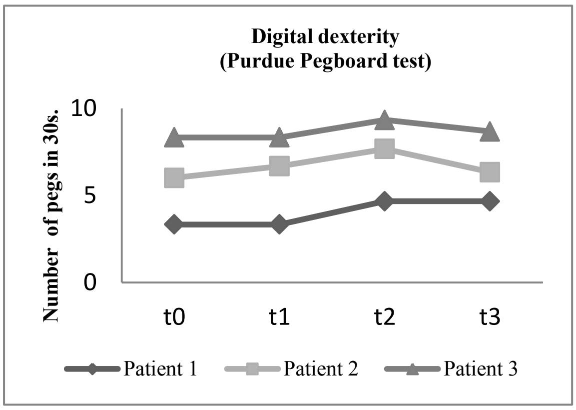

Figure 2. Digital dexterity results of the Purdue Pegboard test of the paretic hand in three hemiparetic chronic stroke patients. Mean number of pegs placed during three 30seconds trials at each of the four evaluations (t0, t1, t2 and t3).

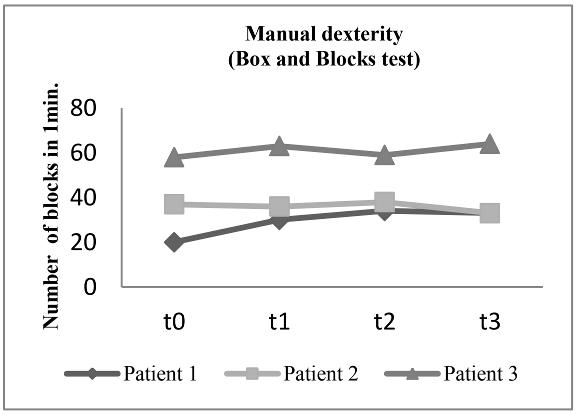

Figure 3. Manual dexterity results of the Box and Blocks test of the paretic hand in three hemiparetic chronic stroke patients. Number of blocks moved from one side to the other side of the box in 1 minute for each of the four evaluations (t0, t1, t2 and t3).

The activity limitation in manual ability during ADL slightly improved for the less performant subject (patient 1, figure 4). Patient 3 was the most performant of the participants but presented a lower result at t2.

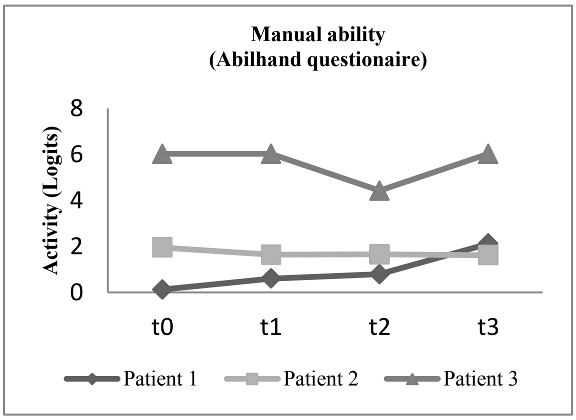

Figure 4. Manual ability observed through the Abilhand questionnaire in three hemiparetic chronic stroke patients. The activity is expressed in Logits in function of the four evaluations (t0, t1, t2 and t3).

During the unilateral grip-lift tasks (in the lab or during fMRI), the participants didn't show bilateral EMG activity of the FDI muscle, reducing the possibility of the presence of mirror movements. Whatever the moment and the place of evaluation (lab or MRI), the bilateral task presented EMG activity of the FDI muscle in both hands, confirming both hands activity. The different grip-lift task parameters analyzed outside the magnet did not change across the various evaluations of the subjects. The parameters previously presented as significantly modified in the paretic hand of chronic stroke subjects compared with healthy controls were the loading phase and the cross-correlation coefficient (Dispa et al., 2013; Chapter III).

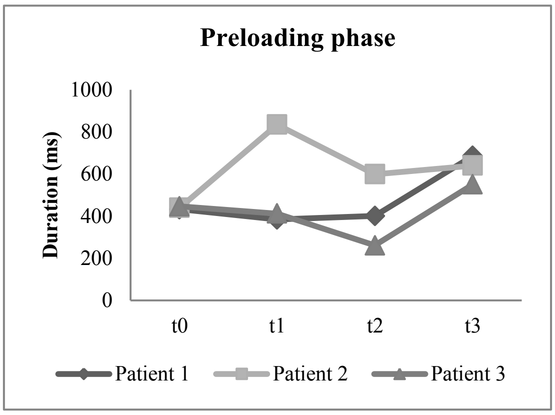

Figure 5. Mean preloading phase of the grip-lift task in sitting position with the paretic hand of three hemiparetic chronic stroke patients. The duration is expressed in milliseconds in function of the four evaluations (t0, t1, t2 and t3).

The duration of the preloading phase and the value of the cross-correlation coefficient did not present clinically significant modifications across the different evaluations (figures 5 and 6).

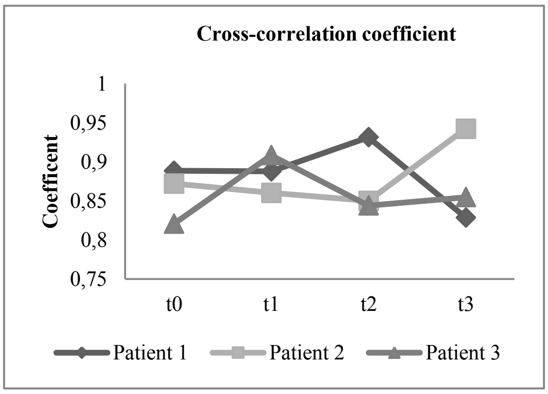

Figure 6. Mean cross-correlation coefficient of the grip-lift task in sitting position with the paretic hand of three hemiparetic chronic stroke patients. The coefficient is expressed in function of the four evaluations (t0, t1, t2 and t3). The y axes begins at 0,75.

fMRI results

Patient 1

In patient 1, the unilateral left hand grip-lift task provided a significant higher activity after treatment in the right M1, S1 and SMA (Bonferoni corrected p-value<0,023) (figure 7 A and B).

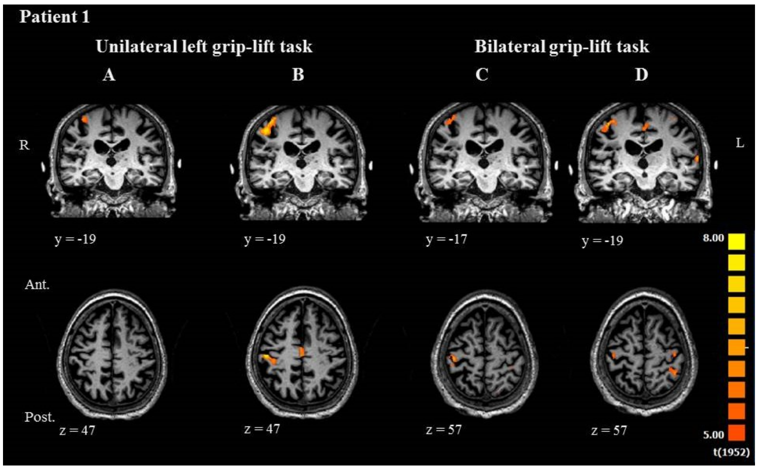

Figure 7. Contrast of brain activity during active minus rest phases of one chronic stroke subject (patient 1). Left paretic hand grip-lift task (A) before and (B) after rehabilitation, and bilateral grip-lift task (C) before and (D) after rehabilitation in Talairach coordinates (all p<0,023; Bonferoni corrected). The first row shows a coronal view and the second row a transversal view. The t-values scale is presented on the right side of the figure. Ant: anterior, Post: posterior, R: right, L: left, y and z: Talairach coordinates.

The related BOLD (blood-oxygen-level dependent) signal presented a double pic of activation after rehabilitation for the unimanual paretic hand grip-lift task in right M1-S1 and SMA (figure 8). At un-corrected p-value<0,0125, an increased activity in the left cerebellum appeared (cluster Talairach coordinates: x = -11, y = -50, z = -18). The bilateral task exhibited essentially a higher activation in S1 of the non-affected left hemisphere and in the SMA (Bonferoni corrected p-value <0,023) (figure 7 C and D). An increase in BOLD signal was observed in the left M1-S1 and SMA during the bilateral grip-lift task after treatment (figure 9).

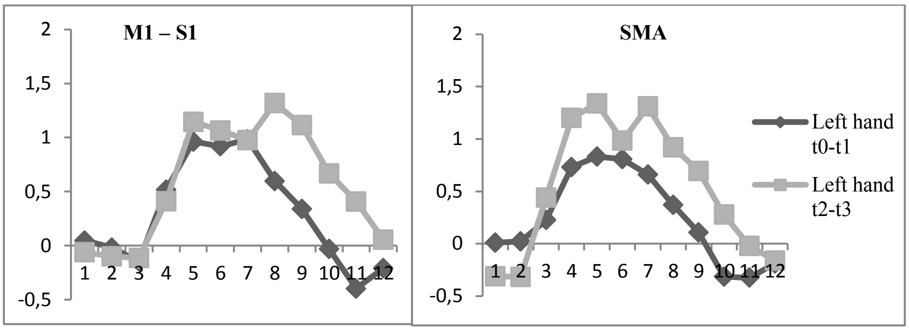

Figure 8. Mean BOLD response of one chronic stroke subject (patient 1) in the left paretic hand grip-lift task. The left panel presents the response in the right M1-S1. The right panel shows the response in the right SMA. The dark grey and light grey traces presented respectively the activity at t_0 in conjunction with t_1 and at t_2 in conjunction with t_3.

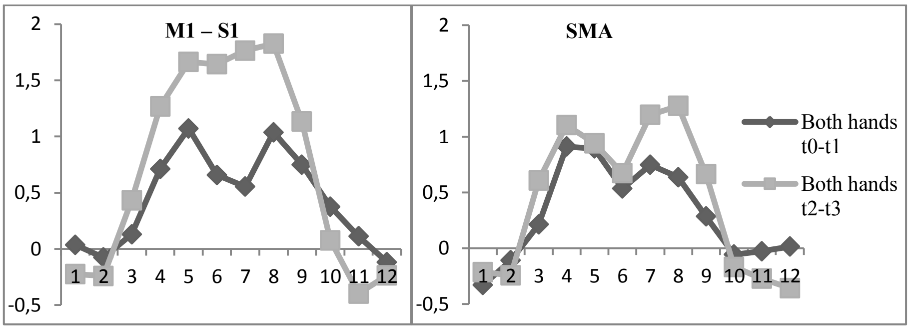

Figure 9. Mean BOLD response of one chronic stroke subject (patient 1) in the bilateral grip-lift task. The left panel presents the response in the right M1-S1. The right panel shows the response in the right SMA. The dark grey and light grey traces presented respectively the activity at t_0 in conjunction with t_1 and at t_2 in conjunction with t_3.

The results of the subtraction between brain activation obtained before and after treatment are provided in table 2. For the unimanual grip-lift task with the left paretic hand, an increased activation was observed after rehabilitation in the left, ipsilateral, Brodmann area 40, as well as, in the right, contralateral, SMA and S1. This last area seemed also to be selectively activated before treatment in the right hemisphere. Before treatment, an activity was also observed in the posterior lobe of the cerebellum bilaterally.

The bilateral grip-lift task presented higher activations after treatment in the left SMA and Brodmann area 40. Before treatment an activity was also seen in the right hemisphere in S1 and M1 (Table 2).

Table 2: Brain activity subtraction before and after treatment during a grip-lift task in patient 1

			mm^3	Coordinates (Talairach)		
Brain region	Side	BA		x	y	z
Unilateral left paretic hand grip-lift task						
More activated areas after treatment						
Postcentral gyrus (S1)	R	3	130	49	-18	42
Paracentral Lobule/Superior frontal gyrus medial (SMA)	R	4/6	332	1	-13	46
Supramarginal gyrus	L	40	172	-54	-23	22
Supramarginal gyrus	L	40	241	-58	-30	36
More activated areas before treatment						
Postcentral gyrus (S1)	R	2	24	39	-35	52
Cerebellum (posterior lobe)	R		30	37	-77	-25
Cerebellum (posterior lobe)	R		21	29	-68	-16
Cerebellum (posterior lobe)	L		16	-10	-83	-24
Cerebellum (posterior lobe)	L		79	-42	-73	-28
Bilateral grip-lift task						
More activated areas after treatment						
Superior frontal gyrus medial (SMA)	L	6	151	0	-11	44
Supramarginal gyrus	L	40	28	-40	-44	37
Supramarginal gyrus	L	40	240	-60	-29	34
More activated areas before treatment						
Postcentral Gyrus (S1)	R	3	22	45	-18	55
Precentral Gyrus (M1)	R	4	31	20	-23	68

Regions activated (All p <0.02, Bonferoni corrected, t=5, minimum 15 voxels/cluster) during unilateral and bilateral grip-lift task. L, left; R, right; BA, Brodmann area; x, y, z, coordinates of peak-height voxels (mm).

Patient 2

The second patient didn't display any significant cortical activity before rehabilitation neither for unilateral paretic hand nor for bilateral grip-lift task (all p-values<0,023; Bonferoni corrected) (figure 10 A and C). After rehabilitation, a higher cortical activity in M1, S1 and small but significant SMA activation was observed in the left hemisphere during the right paretic hand grip-lift task (Bonferoni corrected p-value<0,023) (figure 10 B). The BOLD activity seemed higher after rehabilitation during the unilateral right paretic hand grip-lift task in the left M1-S1 and SMA (figure 11). At un-corrected p-value<0,0125, the right cerebellum (cluster Talairach coordinates: x = 16, y = -51, z = -16) showed an increase in activity. The activation during the bilateral grip-lift task seemed to increase in M1, S1 and SMA in both hemispheres after rehabilitation (Bonferoni corrected p-value<0,023) (figure 10 D). The time course of the BOLD signal in the left M1-S1 and SMA during the unilateral and bilateral grip-lift task before and after rehabilitation is presented respectively in figure 11 and 12, showing the increased activity in these areas after rehabilitation.

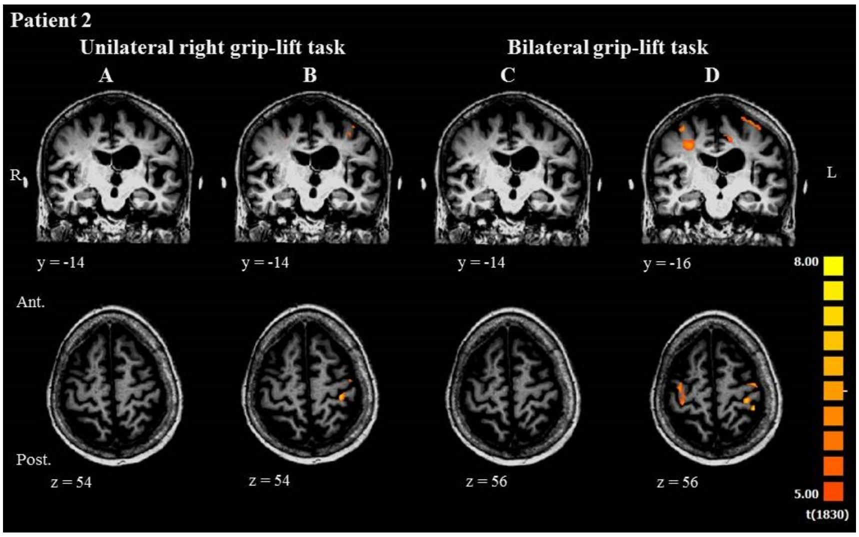

Figure 10. Contrast of brain activity during active minus rest phases of one chronic stroke subject (patient 2). Right paretic hand grip-lift task (A) before and (B) after rehabilitation, and bilateral grip-lift task (C) before and (D) after rehabilitation in Talairach coordinates (all p<0,023; Bonferoni corrected). The first row shows a coronal view and the second row a transversal view. The t-values scale is presented on the right side of the figure. Ant: anterior, Post: posterior, R: right, L: left, y and z: Talairach coordinates.

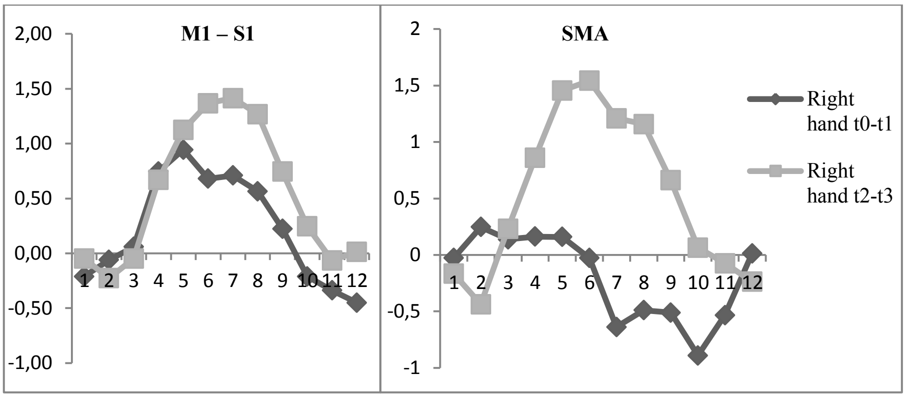

Figure 11. Mean BOLD response of one chronic stroke subject (patient 2) in the right paretic hand grip-lift task. The left panel presents the response in the left M1-S1. The right panel shows the response in the left SMA. The dark grey and light grey traces presented respectively the activity at t_0 in conjunction with t_1 and at t_2 in conjunction with t_3.

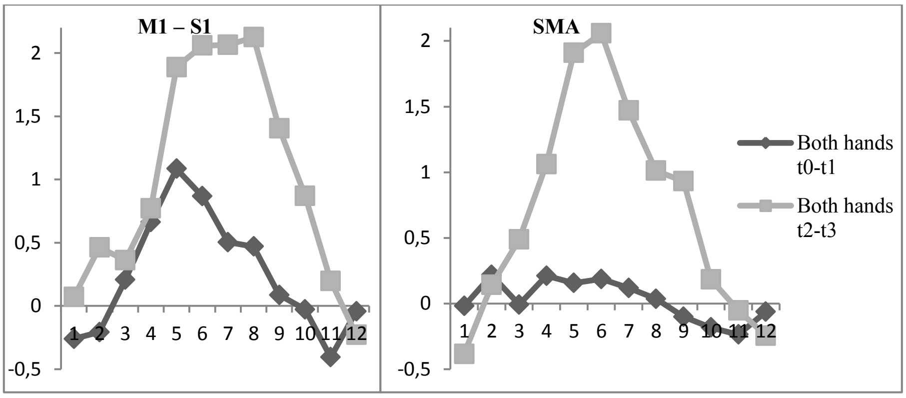

Figure 12. Mean BOLD response of one chronic stroke subject (patient 2) in the bilateral grip-lift task. The left panel presents the response in the left M1-S1. The right panel shows the response in the left SMA. The dark grey and light grey traces presented respectively the activity at t_0 in conjunction with t_1 and at t_2 in conjunction with t_3.

Table 3 presents the results of the subtraction between brain activation obtained before and after treatment during the unilateral right paretic hand grip-lift task. An increased activity was seen after treatment in the ipsilateral PM, Brodmann area 7 and posterior lobe of the cerebellum. The contralateral hemisphere presented an increase of activity after rehabilitation in M1, S1, PM, cuneus and Brodmann area 31. Before treatment a selective activity was observed in bilateral Brodmann area 18, right lingual gyrus and cerebellum (Table 3).

Table 3: Brain activity subtraction before and after treatment during the unilateral right paretic hand grip-lift task in patient 2

Brain region	Side	BA	mm^3	Coordinates (Talairach) x	y	z
Unilateral right paretic hand grip-lift task						
More activated areas after treatment						
Middle Frontal Gyrus (PM)	R	6	73	26	-13	38
Precuneus	R	7	39	26	-52	40
Superior Parietal Lobule	R	7	15	17	-56	60
Postcentral Gyrus (S1)	L	2	15	-25	-35	66
Precentral Gyrus (M1)	L	4	86	-32	-28	54
Precentral Gyrus (PM)	L	6	126	-49	-5	32
Cuneus	L	18	67	-6	-85	13
Paracentral Lobule	L	4	34	-5	-23	46
Cingulate Gyrus	L	31	26	-8	-37	33
Cerebellum (posterior lobe)	R		16	41	-41	-35
More activated areas before treatment						
Inferior Occipital Gyrus	R	18	60	36	-86	-6
Lingual Gyrus	R	17	314	21	-98	-10
Lingual Gyrus	R	18	16	7	-96	-10
Lingual Gyrus	L	18	59	-5	-99	-13
Cerebellum (posterior lobe)	R		52	28	-74	-33

Regions activated (All $p < 0.016$, Bonferoni corrected, t=5, minimum 15 voxels/cluster). L, left; R, right; BA, Brodmann area; x, y, z, coordinates of peak-height voxels (mm).

In table 4, the subtraction of the cortical activity before and after rehabilitation is presented for the bilateral grip-lift task. Increased activation was observed after treatment in both hemispheres mainly in M1, SMA and cerebellum, as well as, in left S1.

Table 4: Brain activity subtraction before and after treatment during the bilateral grip-lift task for patient 2

			mm^3	Coordinates (Talairach)		
Brain region	Side	BA		X	y	z
Bilateral grip-lift task						
More activated areas after treatment						
Precentral Gyrus (M1)	R	4	140	36	-17	55
Precentral Gyrus (M1)	R	4	135	24	-21	63
Precentral gyrus (M1)	R	4	145	7	-28	71
Precuneus	R	7	109	24	-51	38
Precuneus	R	7	115	24	-63	26
Lingual Gyrus	R	18	103	21	-58	3
Cuneus	R	18	158	18	-75	25
Inferior Temporal Gyrus	R	21	312	58	-8	-13
Superior Temporal Gyrus	R	22	376	50	-38	11
Superior frontal gyrus	R	6	137	18	-3	42
Parahippocampal Gyrus	R	30	92	32	-50	7
Large bilateral area with 3 peaks	R		4496	14	-23	40
Precental/postcentral gyrus	R	4/2				
Cingulate gyrus/Paracentral lobule	R	31/4				
Cingulate gyrus/Paracentral lobule	L	31/4				
Fusiform Gyrus	R	37	689	54	-48	-15
Inferior Temporal Gyrus	R	37	125	46	-68	-1
Postcentral Gyrus (S1)	L	2	226	-29	-36	62
Precentral Gyrus (M1)	L	4	149	-31	-29	55
Precentral Gyrus (M1)	L	4	93	-38	-14	54
Paracentral lobule	L	4	271	-5	-24	67
Lingual Gyrus	L	18	516	-3	-90	-15
Middle Occipital Gyrus	L	18	596	-12	-90	11
Cuneus	L	18	381	-14	-80	21
Fusiform Gyrus	L	19	391	-19	-64	-8
Middle Occipital Gyrus	L	19	389	-29	-85	8
Superior frontal gyrus medial (SMA)	L	6	168	-4	2	43
Lingual gyrus	L	18	453	-17	-66	5
Cerebellum (anterior lobe)	R		1357	41	-53	-29
Cerebellum (anterior lobe)	R		138	4	-66	-4
Cerebellum (posterior lobe)	R		105	35	-65	-22
Cerebellum (posterior lobe)	R		329	14	-76	-40
Cerebellum (anterior lobe)	L		143	-5	-49	-8
Cerebellum (posterior lobe)	L		98	-24	-37	-39
Cerebellum (posterior lobe)	L		92	-47	-49	-24

Regions activated (All p <0.016, Bonnferoni corrected, t=5, minimum 15 voxels/cluster). L, left; R, right; BA, Brodmann area; x, y, z, coordinates of peak-height voxels (mm).

Patient 3

During the unilateral right paretic hand grip-lift task, patient 3 presented an increase of activation in the left M1, S1, SMA and the right cerebellum after training (all p-value<0.023; Bonferoni corrected) (figure 13 A, B and C).). The BOLD time course presented a clear double peak both before and after training in M1-S1, SMA and cerebellum, and seemed slightly higher after rehabilitation (figure 14). During the bilateral grip-lift task, a high cortical activity was observed in motor areas (Bonferoni corrected p-value<0,001) (figure 13 D). This activation was increased after training in M1, S1 and SMA in both hemispheres (Bonferoni corrected p-value <0,001) (figure 13 E). The related BOLD signal was higher after rehabilitation for the bimanual grip-lift task in left M1-S1 and SMA (figure 15).

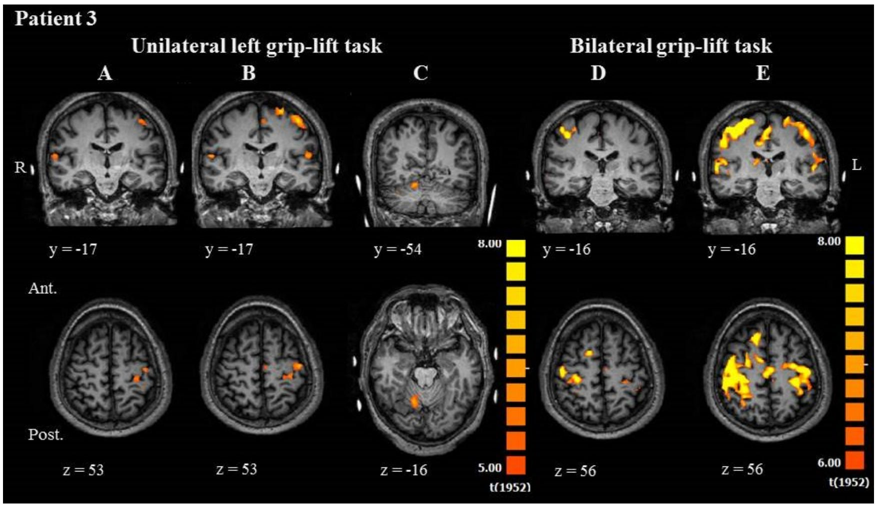

Figure 13. Contrast of brain activity during active minus rest phases of one chronic stroke subject (patient 3). Right paretic hand grip-lift task (A) before and (B and C) after rehabilitation, and bilateral grip-lift task (D) before and (E) after rehabilitation in Talairach space (all p<0,023; Bonferoni corrected). The first row shows a coronal view and the second row a transversal view. The t-values scale is presented on the right side of the three first columns for the unilateral grip-lift task and on the right side of the two last columns for the bilateral task. Ant: anterior, Post: posterior, R: right, L: left, y and z: Talairach coordinates.

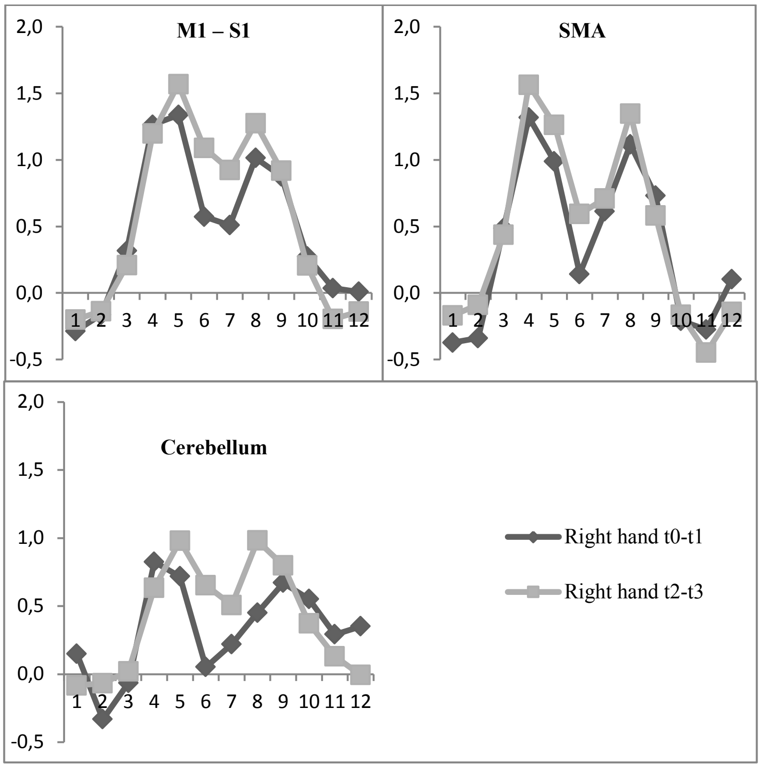

Figure 14. Mean BOLD response of one chronic stroke subject (patient 3) in the right paretic hand grip-lift task. The left panel presents the response in the left M1-S1. The middle panel shows the response in the left SMA. The right panel presents the BOLD signal in the right cerebellum. The dark grey and light grey traces presented respectively the activity at t_0 in conjunction with t_1 and at t_2 in conjunction with t_3.

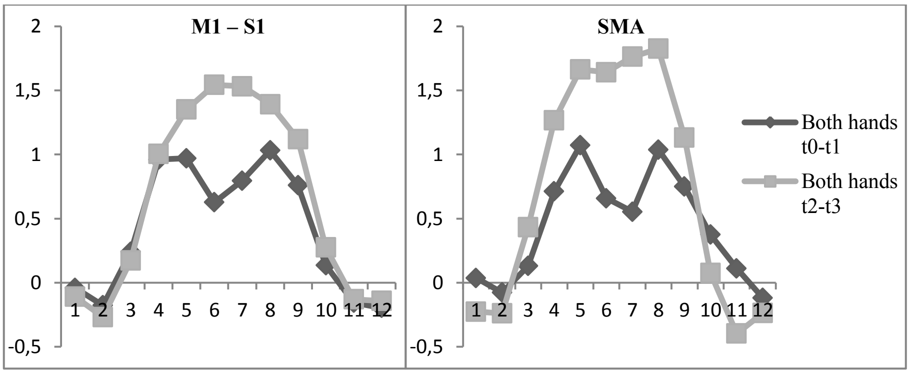

Figure 15. Mean BOLD response of one chronic stroke subject (patient 3) in the bilateral grip-lift task. The left panel presents the response in the left M1-S1. The right panel shows the response in the left SMA. The dark grey and light grey traces presented respectively the activity at t_0 in conjunction with t_1 and at t_2 in conjunction with t_3.

Table 5 presents the subtraction of the brain activity before and after rehabilitation for patient 3 during an unilateral right paretic hand grip-lift task. An augmented activity was observed in both hemispheres in the cerebellum and Brodmann area 47. Additionally, in the ipsilateral hemisphere the thalamus, hippocampus, Brodmann area 46 and 10 were more activated after treatment. In the contralateral side the PM presented increased activation.

Table 5: Brain activity subtraction before and after treatment during an unilateral right paretic hand grip-lift task in patient 3

			mm^3	Coordinates (Talairach)		
Brain region	Side	BA		x	Y	Z
Unilateral right paretic hand grip-lift task						
More activated areas after treatment						
Inferior Frontal Gyrus	R	46	68	44	41	4
Inferior Frontal Gyrus	R	46	62	41	37	13
Inferior Frontal Gyrus	R	47	32	39	24	-6
Inferior Frontal Gyrus	R	47	24	26	18	-23
Medial Frontal Gyrus	R	10	29	16	57	3
Superior Frontal Gyrus (PM)	L	6	113	-13	-10	64
Middle Frontal Gyrus	L	9	157	-22	39	34
Precentral Gyrus (PM)	L	6	31	-23	-20	66
Inferior Frontal Gyrus	L	47	27	-34	26	-15
Inferior Frontal Gyrus	L	47	70	-53	18	0
Thalamus (anterior nucleus)	R		18	6	-4	12
Hippocampus	R		122	27	-11	-15
Cerebellum (anterior lobe)	R		188	34	-48	-25
Cerebellum (anterior lobe)	R		15	26	-35	-24
Cerebellum (anterior lobe)	R		307	16	-50	-19
Cerebellum (posterior lobe)	R		81	4	-69	-22
Cerebellum (anterior lobe)	L		32	-3	-44	-3
Cerebellum (anterior lobe)	L		23	-3	-60	-21

Regions activated (All $p < 0.05$, Bonnferoni corrected, t=4,87, minimum 15 voxels/cluster). L, left; R, right; BA, Brodmann area; x, y, z, coordinates of peak-height voxels (mm).

Table 6 presents the subtraction of the brain activity before and after rehabilitation during the bilateral grip-lift task. An important increase of activation was observed bilaterally after treatment, especially in M1, S1, PM, thalamus and cerebellum, as well as in the auditory areas and in the parts of cortex involved in planning (Brodmann areas 7, 8, 9 and the cingulate cortex). Additionnally, in the right hemisphere the putamen was more activated after treatment and in the left side the SMA and the caudate body presented an increase of activity after rehabilitation.

Table 6: Brain activity subtraction before and after treatment during a bilateral grip-lift task for patient 3

			mm^3	Coordinates (Talairach)		
Brain region	Side	BA		X	y	z
Bilateral grip-lift task						
More activated areas after treatment						
Postcentral Gyrus (S1)	R	2	101	52	-19	33
Postcentral Gyrus (S1)	R	2	21	39	-27	38
Postcentral Gyrus (S1)	R	2	150	37	-23	30
Precentral Gyrus (M1)	R	4	3801	37	-18	51
Precentral Gyrus (PM)	R	6	26	56	-1	31
Precentral Gyrus (PM)	R	6	24	40	2	26
Superior frontal gyrus (PM)	R	6	592	18	-10	54
Superior Frontal Gyrus (PM)	R	6	33	21	-10	63
Superior Frontal Gyrus (PM)	R	6	100	15	12	54
Superior Frontal Gyrus (PM)	R	6	109	16	20	50
Superior Parietal Lobule	R	7	113	28	-57	46
Precuneus	R	7	46	23	-47	49
Precuneus	R	7	261	12	-55	60
Paracentral lobule	R	5	62	5	-33	44
Middle Frontal Gyrus	R	8	35	29	22	42
Superior Frontal Gyrus	R	8	299	15	38	42
Middle Frontal Gyrus	R	9	222	39	31	26
Middle Frontal Gyrus	R	9	18	28	34	38
Middle Frontal Gyrus	R	10	306	38	46	8
Middle Frontal Gyrus	R	10	78	37	54	18
Superior Frontal Gyrus	R	10	540	27	42	26
Medial Frontal Gyrus	R	10	199	16	47	2
Middle Frontal Gyrus	R	11	16	28	46	-7
Sub-Lobar, Extra-Nuclear	R	13	440	39	11	-12
Insula	R	13	93	41	-19	-2
Insula	R	13	21	40	-1	5
Temporal Lobe, Sub-Gyral	R	21	87	46	-12	-14
Superior Temporal Gyrus	R	22	112	51	7	0
Parahippocampal Gyrus	R	28	63	21	-11	-20
Posterior Cingulate	R	29	18	2	-42	13

Anterior Cingulate	R	32	68	26	35	10
Anterior Cingulate	R	32	125	18	33	16
Anterior Cingulate	R	32	47	8	38	8
Anterior Cingulate	R	33	22	6	21	20
Parahippocampal Gyrus	R	35	18	24	-14	-24
Inferior Parietal Lobule	R	40	2384	51	-38	37
Inferior Parietal Lobule	R	40	16	38	-40	49
Inferior Parietal Lobule	R	40	1280	31	-39	37
Superior Temporal Gyrus	R	42	67	60	-25	8
Superior Temporal Gyrus	R	42	27	59	-28	16
Postcentral Gyrus	R	43	557	56	-7	12
Postcentral Gyrus	R	43	354	51	-17	15
Inferior Parietal Lobule	R	45	609	48	25	0
Superior Temporal Gyrus	R	22	57	47	-22	2
Postcentral Gyrus (S1)	L	3	33	-30	-26	45
Postcentral Gyrus (S1)	L	3	35	-34	-30	49
Precentral Gyrus (M1)	L	4	219	-27	-27	59
Precentral Gyrus (M1)	L	4	204	-35	-21	59
Precentral Gyrus (M1)	L	4	272	-36	-15	48
Precentral Gyrus (M1)	L	4	20	-35	-15	36
Superior Frontal Gyrus (SMA)	L	6	229	-8	-5	62
Superior Frontal Gyrus (SMA)	L	6	41	-10	10	52
Precentral Gyrus (PM)	L	6	70	-22	-20	66
Superior Parietal Lobule	L	7	33	-3	-65	60
Precuneus	L	7	18	-4	-58	63
Superior Parietal Lobule	L	7	52	-22	-57	60
Superior Parietal Lobule	L	7	55	-33	-50	59
Superior Frontal Gyrus	L	8	659	-7	33	45
Middle Frontal Gyrus	L	8	17	-23	24	45
Superior Frontal Gyrus	L	9	33	-12	46	31
Superior Frontal Gyrus	L	10	121	-19	40	16
Middle Frontal Gyrus	L	9	565	-26	40	35
Precentral gyrus	L	6	274	-50	7	5
Anterior Cingulate	L	24	35	-6	36	3
Cingulate Gyrus	L	24	16	-7	7	31
Anterior Cingulate	L	32	20	-2	43	5
TransverseTemporal Gyrus	L	41	36	-49	-20	7
Precentral Gyrus	L	6	32	-53	-5	10
Cerebellum (anterior lobe)	R		22	39	-43	-27
Cerebellum (anterior lobe)	R		161	11	-55	-17
Cerebellum (posterior lobe)	R		520	2	-65	-20
Putamen	R		1124	23	1	16
Putamen	R		16	30	-14	10
Thalamus	R		85	7	-16	16
Cerebellum (anterior lobe)	L		639	-9	-45	-11
Cerebellum (posterior lobe)	L		80	-31	-39	-42
Caudate Body	L		23	-20	-12	30
Caudate Body	L		49	-20	-1	26
Culmen	L		250	-24	-46	-21
Thalamus	L		195	-12	-10	16

More activated areas before treatment						
Precentral Gyrus (PM)	R	6	46	59	-15	44
Precentral Gyrus (PM)	R	6	23	59	-1	39
Postcentral Gyrus *Outside the brain*	R		68	25	-47	70

Regions activated (All p <0.05, Bonnferoni corrected, t=4,87, minimum 15 voxels/cluster). L, left; R, right; BA, Brodmann area; x, y, z, coordinates of peak-height voxels (mm).

Before treatment an increase of activity in the right hemisphere was seen in a part of the PM compared to the “after treatment” activation (Table 6).

DISCUSSION

This preliminary study permits to test the fMRI compatible setup described in Chapter IV section 1 within a chronic stroke population. Additionally, our data complete the evaluation of the effect of a bilateral rhythmic auditory cued grip-lift rehabilitation described in Chapter III. As previously shown (see chapter III), the grip-lift task parameters, which presented a significant modification in the paretic hand of chronic stroke subjects compared to healthy controls, did not show any adaptation through the treatment.

The low number and the heterogeneity of the subjects conducted us to observe the results at t0 and t1, as well as, t2 and t3 in conjunction. This specification assumes that the participants had already started to recover at t2 but doesn’t allow to demonstrate any greater improvement at t3.

For the unilateral grip-lift task with the paretic hand, all patients presented a greater activation of motor areas (M1, S1, PM or SMA) after rehabilitation. For the first subject, bilateral increased activation was seen after rehabilitation. The two right hemiparetic patients presented an increased activity in PM after treatment. Patient 2 also presented a bilateral increase in S1 and M1. Patient 3 increased the activity in the cerebellum but also in some areas involved in planification and memory in the right hemisphere (Brodmann area 10 and 46). The higher initial level and the higher increase of activation after rehabilitation in both the injured and unaffected hemisphere were observed in patient 3. Indeed, this patient was the youngest but also the most performant in terms of digital dexterity, manual dexterity and manual ability.

Some authors suggest that bilateral motor tasks involve more brain regions and a higher cortical activity than unilateral lower-limb movements (Noble et al., 2014). In the latter study, the subjects were asked to realize the action through a plantar ankle flexion. This is consistent with previous studies focusing on the upper-limb cyclic movements (Swinnen and Wenderoth, 2004). Those results should be confirmed in a non-rythmic grip-lift task. It appears logical that in our study, the small population of heterogeneous hemiparetic chronic stroke patients did not show clearly similar results before rehabilitation.

After rehabilitation, we observed for each subject a higher number of involved areas mainly for the bilateral movements. These results represent some different adaptations of the brain activity after therapy. For unimanual movements, there was some increase of brain activity in contralateral motor areas (lesioned hemisphere), and particularly in areas S1 or M1 in patients 1 and 2, SMA in patient 1, and PM in patients 2 and 3. Additionally, patient 3 presented, in unilateral movements, an augmented activity in multiple areas including memory and planification areas. In bilateral tasks, patient 1 presented an augmented brain activity after treatment in left (non-lesioned hemisphere) SMA and Brodmann area 40. For the two right hemiparetic patients (subject 2 and 3) performing bilateral movements, numerous areas with increased activation after therapy were observed including bilateral M1, S1, PM and the cerebellum, as well as left SMA. Our results require corroboration in a large population.

The principal areas described in bimanual coordination in healthy adults are the cerebellum, SMA (with often extends to the posterior cingulate motor area - CMA), and PM (premotor cortex) (Swinnen and Wenderoth, 2004).

These areas were not systematically observed before rehabilitation in our chronic stroke patients. Furthermore, after rehabilitation, some of those areas were more active (principally SMA and the cerebellum) but not all of them. Two hypotheses could be made: first, as a result of the lesion, the subject’s brain didn’t act as healthy controls. Secondly, the bimanual task was in phase and probably not challenging enough to highlight all those areas. In fact, the synchrony or asynchrony of the movement seems to modify which cerebellum area is activated (Swinnen and Wenderoth, 2004). Additionnally, in more demanding coordination tasks, the PMV activation appears to change. Future studies should explore and help to gain a better understanding of this activity patterns.

Further, the mean BOLD response presented a double peak which was even more relevant after therapy which suggests normalization of the signal time course.

Indeed, a double peak of activation was previously described in healthy adults in the literature (Kuhtz-Buschbeck et al., 2001). Those temporary increases of the fMRI signal should be related to the dynamic phases of lifting and putting the manipulandum down.

In the present study, the use of a compatible manipulandum and EMG recording material permit to verify if the requested task is done (i.e. Grip, lift and release following the instructions, unilateral or bilateral muscle activity during respectively unimanual or bimanual tasks). In further works, it could be interesting to observe the evolution of the grip-lift task across the evaluations during fMRI acquisition as well as to add the measured parameters as a covariate for fMRI analysis.

In conclusion, in this hemiparetic chronic stroke studied population, the rehabilitation period obviously modifies the cortical activity related to either unilateral or bilateral grip-lift tasks. These data displayed even without any clinical significant functional improvement. Our findings indicate that the patient's subjective perception of fluentness and easiness after rehabilitation could be related to early cortical activity adaptation.

A larger study classifying chronic stroke patients in different categories with respect to the site of lesion, the functional recovery and the results of at least another cortical mapping technique such as TMS could be interesting to confirm our results (Eliassen et al., 2008).

APPENDIX B: ABILHAND questionnaire

Penta et al., 2001; www.rehab-scales.org

The ABILHAND questionnaire was developed as a measure of manual ability as perceived by the patient. It explores the most representative inventory of manual activities. Some items were selected from existing scales; others were devised to extend the range of activities. The first application of the questionnaire in a sample of rheumatoid arthritis patients (*Arch Phys Med Rehabil 1998; 79: 1038-42*) showed that the items defined a valid manual ability scale. A second application of the questionnaire in a larger sample of chronic stroke patients showed that the unimanual activities (usually realized with one hand) were too easy for the patients. So, a subset of 23 bimanual activities (usually realized with two hands) has been retained and calibrated for chronic stroke patients (*Stroke 2001; 32: 1627-34*). ABILHAND was originally developed using the Rasch measurement model. It allows to convert ordinal scores into linear measures located on a unidimensional scale.

Procedures

The ABILHAND questionnaire is administered on an interview basis (patients do not realize the activities). Patients are asked to estimate the ease or difficulty in performing each activity, when the activities are done:

- Without other technical or human help (even if the patient actually uses help in daily life);
- Irrespective of the limb(s) actually used to do the activity;
- Whatever the strategy used (any compensation is allowed).

During the evaluation, a 3-level response scale is presented to the patients. Patients are asked to rate their perception on the response scale as either "Impossible", "Difficult" or "Easy". Activities not attempted in the last 3 months are not scored and are entered as missing responses (tick the question mark). For any activity the four potential answers are:

- ***Impossible***: the patient is unable to perform the activity without using any other help;
- ***Difficult***: the patient is able to perform the activity without any help but experiences some difficulty;
- ***Easy***: the patient is able to perform the activity without any help and experiences no difficulty;
- ***Question mark***: the patient cannot estimate the difficulty of the activity because he/she has never done the activity. Note that when a patient has never attempted the activity, the rater needs to make sure why it is so. If an activity was never attempted because it is impossible, then it must be scored as "Impossible" rather than "Question mark".

The instructions are given to the patient only at the beginning of the test. Five items are used for training in order to help the patient in feeling each level of the rating scale and in using the whole amplitude of the response scale. The subsequent activities are neither preceded nor followed by any instruction. The examiner can repeat the instructions whenever the patient shows some hesitation in answering.

Activities order

The activities of the ABILHAND questionnaire are presented in a random order to avoid any systematic effect. Ten different random orders of presentation are used. The rater must select the next one of the 10 orders for each new assessment, no matter which patient is tested.

ABILHAND - Manual Ability Measure
English version

Patient ______________________________ **Date** _____________

	How **DIFFICULT** are the following activities?	Impossible	Difficult	Easy	?
1.	Pulling up the zipper of trousers				
2.	Peeling onions				
3.	Sharpening a pencil				
4.	Taking the cap off a bottle				
5.	Filing one's nails				
6.	Peeling potatoes with a knife				
7.	Buttoning up trousers				
8.	Opening a screw-topped jar				
9.	Cutting one's nails				
10.	Tearing open a pack of chips				
11.	Unwrapping a chocolate bar				
12.	Hammering a nail				
13.	Spreading butter on a slice of bread				
14.	Washing one's hands				
15.	Buttoning up a shirt				
16.	Threading a needle				
17.	Cutting meat				
18.	Wrapping up gifts				
19.	Fastening the zipper of a jacket				
20.	Fastening a snap (jacket, bag, ...)				
21.	Shelling hazel nuts				
22.	Opening mail				
23.	Squeezing toothpaste on a toothbrush				

APPENDIX C: SATIS-Stroke questionnaire

Bouffioulx et al., 2008

The SATIS-Stroke questionnaire was developed as a measure of satisfaction with activities and participation as perceived by the patient. It explores the most representative inventory life situations. Some items were selected from existing scales. The first application of the questionnaire in a sample of stroke patients showed that the items defined a valid satisfaction scale. SATIS-Stroke was originally developed using the Rasch measurement model. It allows converting ordinal scores into linear measures located on a unidimensional scale.

Procedures

The SATIS-Stroke questionnaire is administered on an interview basis (patients do not realize the activities) or self administration. Patients are asked to estimate the satisfaction level in performing each life situation, when the activities/participation are done:

- In the month preceding the filling out the questionnaire;
- With other technical or human help (even if the patient actually uses help in daily life);
- Whatever the strategy used (any compensation is allowed).

During the evaluation, a 4-level response scale is presented to the patients. Patients are asked to rate their perception on the response scale as either "Very dissatisfied", "Dissatisfied", “Satisfied” or "Very satisfied". Activities or participation not attempted in the last month are not scored and are entered as missing responses (tick the question mark). For any activity the four potential answers are:

- ***Very dissatisfied:*** the patient expresses a deep dissatisfaction with the way it carries out the activity or socially takes part in the various life situations, whatever the strategy used, or the fact of not being able to carry it out taking into account the circumstances;

- ***Dissatisfied:*** the patient expresses a dissatisfaction with the way it carries out the activity or socially takes part in the various life situations, whatever the strategy used, or the fact of not being able to carry it out taking into account the circumstances;
- ***Satisfied:*** the patient expresses satisfaction in the achievement of the activity or socially takes part, but estimates not to enjoy the full satisfaction taking into account the circumstances;
- ***Very satisfied:*** the patient expresses a complete satisfaction in both the level of achievement, that of social participation.
- ***Question mark:*** the patient either cannot express his level of satisfaction in the achievement or the social participation or did not perform or did not take part in the various situations of life.

The instructions are given to the patient only at the beginning of the test. Five items are used for training in order to help the patient in feeling each level of the rating scale and in using the whole amplitude of the response scale. The subsequent activities are neither preceded nor followed by any instruction. The examiner can repeat the instructions whenever the patient shows some hesitation in answering.

Activities order

The activities of the SATIS-Stroke questionnaire are presented in a random order to avoid any systematic effect. Ten different random orders of presentation are used. The rater must select the next one of the 10 orders for each new assessment, no matter which patient is tested.

Patient____________________________ **Date**__________________

	Are you **SATISFIED** in the performing of the following life situations (i.e. not priority to change)?	Very dissatisfied	Dissatisfied	Satisfied	Very satisfied	?
01	Participating in food and drink preparation in all circumstance					
02	Using knife, fork and spoon in all circumstance					
03	Participating in spoken exchange of information with your entourage					
04	Washing your hairs according to your needs					
05	Undressing to use the toilet and redressing in your home or outside of this one					
06	Making your personal hygiene according to your needs					
07	Having an urinary continence in your home and outside of this one					
08	Participating in arts and culture (cinema, theatre, etc.)					
09	Co-operating with your entourage					
10	Reading and understanding a document in all circumstance					
11	Using telephone at home according to your needs					
12	Listening to and looking at television according to your needs					
13	Managing your incomes in all circumstance					
14	Using coins and banknotes in all circumstance					
15	Dressing and undressing in all circumstance and according to your needs					
16	Ensuring that your rights are respected					
17	Participating in spousal relationships					
18	Taking your bath or your shower according to your needs					
19	Reaching objects in your closely space					
20	Getting clothes out of the closet					
21	To supplement administrative documents in all circumstance					
22	Moving inside your home					
23	Moving outside your home in all circumstance					
24	Climbing and going downstairs all stages in your home according to your needs					

	Are you **SATISFIED** in the performing of the following life situations (i.e. not priority to change)?	Very dissatisfied	Dissatisfied	Satisfied	Very satisfied	?
25	Entering and exiting your home according to your needs					
26	Opening and closing doors in your home					
27	Using storage spaces in your house					
28	Choosing appropriate clothes					
29	Getting in feeling across					
30	Being aware with what surrounds you					
31	Expressing oneself to someone					
32	Participating in ceremonies (mariage, gathering family, etc.)					
33	Asking for help in an emergency situation					
34	Managing your pains in all circumstance					
35	Maintaining emotional relationships					
36	Having a sexual relationship with another					

SUMMARY

This thesis aims to advance the evaluation and rehabilitation of precision grip in chronic stroke patients. Stroke is a leading cause of permanent deficits worldwide, and fine manipulation skills are often disturbed in the paretic hand.

The evaluation of predictive and reactive control in this population highlighted deficits in the paretic hand under both conditions. Patients also displayed a significant decrease in digital dexterity and an increase in the time taken to lift the manipulandum with the paretic hand compared with the non-paretic hand and control subjects. A specific rhythmic bilateral grip-lift task oriented therapy undertaken three times per week for 8 weeks did not modify grip-lift task parameters, digital dexterity, manual ability or subjects' satisfaction with their participation in activities of daily living. Patients' perceptions of increased ease and fluency of manipulation after therapy was not measured through these evaluations. The suggestion of changes in cortical activity related to the task led us to develop a fMRI compatible manipulandum and concomitant EMG recording setup. With a specific evaluation protocol, this proved to be accurate at least in healthy adults. Nevertheless, there are limitations to the fMRI method. Two of them are the subjects' supine position and the restriction of their view of the manipulated object during image acquisition. These parameters have been shown to influence grip-lift task performance in healthy adults. There is a strong recommendation to consider position and view during rehabilitation and to assess the patient under the same conditions during fMRI. The literature also recommends adding at least one further brain mapping technique to complete the evaluation.

In conclusion, chronic stroke subjects have manipulation disabilities that should be considered for rehabilitation. There is a strong need to combine structure and function specific evaluation in determining which type of therapy is appropriate for each patient in terms of functional recovery level, cortical lesion site and cortical excitability.

RESUME

Cette thèse vise à préciser l'évaluation et la rééducation de la pince de précision chez le patient au stade chronique après un accident vasculaire cérébral (AVC). En effet, l'AVC est une des causes principales de déficit permanent dans le monde, de plus, la manipulation fine est régulièrement perturbée dans la main parétique chez ces sujets.

L'évaluation du contrôle prédictif et réactif de la prise de précision dans cette population montre un déficit de la main parétique. Ces patients montrent également une diminution significative de la dextérité digitale et une augmentation du délai nécessaire pour soulever un objet avec la main parétique en comparaison à la main non-parétique ou main dominante de sujets contrôles. Une thérapie spécifique, rythmique, bilatérale, orientée sur la tâche de levé-déposé réalisée trois fois par semaine pendant 8 semaines ne modifie pas les paramètres du levé-déposé, la dextérité digitale, l'habilité manuelle ou la satisfaction du sujet dans leur participation aux activités de la vie de tous les jours. L'impression subjective de fluidité et facilité des manipulations après le traitement ne fût pas reflétée par l'évaluation. La suggestion de changements de l'activité corticale liée à la tâche nous a conduits à développer un manipulandum compatible avec l'imagerie par résonance magnétique fonctionnelle (fMRI) conjointement avec l'enregistrement électromyographique. Un protocole d'évaluation et un matériel spécifique sont décrits comme adéquat chez l'adulte sain. Cependant, certaines limitations liées à la méthode d'acquisition fMRI, telles que la position couchée et les restrictions de vision de l'objet manipulé, doivent être prises en compte. En effet, ces paramètres ont montré une influence sur la performance du levé-déposé chez l'adulte sain. Il est recommandé de prendre en compte la position et la vision lors de la rééducation des patients et d'évaluer sous les mêmes conditions en fMRI. De plus, la littérature recommande l'ajout d'une technique supplémentaire de cartographie cérébrale pour compléter l'évaluation.

En conclusion, les sujets post-AVC au stade chronique présentent des troubles de la manipulation qui devraient être pris en compte lors de la rééducation.

Il est nécessaire de combiner l'évaluation des structures et des fonctions dans le but de déterminer le type de thérapie approprié à chaque patient selon son degré de récupération fonctionnelle, le site de la lésion et l'excitabilité corticale.

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