

Correlation between impaired dexterity and corticospinal tract dysgenesis in congenital hemiplegia

Julie Duque,¹ Jean-Louis Thonnard,² Yves Vandermeeren,¹ Guillaume Sébire,³ Guy Cosnard⁴ and Etienne Olivier¹

¹Laboratory of Neurophysiology, ²Physical Medicine and Rehabilitation Unit, ³Department of Neuropediatrics and ⁴Neuroradiology Department, School of Medicine, Université catholique de Louvain, Brussels, Belgium

Correspondence to: Professor Etienne Olivier, Laboratory of Neurophysiology, School of Medicine, Université catholique de Louvain, 54 avenue Hippocrate, B-1200 Brussels, Belgium
E-mail: olivier@nefy.ucl.ac.be

Summary

One of the most devastating consequences of early corticospinal lesions is the impaired dexterity that results in a noticeable deficit while manipulating small objects. One purpose of the present study was to investigate the extent to which a deficit in the coordination of fingertip forces when grasping and lifting an object between the thumb and index finger could account for the impaired dexterity in patients with congenital hemiplegia (CH). A second objective was to examine whether, in these patients, deficits in skilled hand movements are correlated with the importance of structural damage to the corticospinal tract. The scaling and coordination of fingertip forces during precision grip was investigated in 16 CH patients (aged 8–19 years) and 16 age- and sex-matched control subjects. Proprioception, stereognosis, pressure sensitivity and motor upper limb function (including digital and manual dexterity) were also assessed quantitatively. The structural damage of the corticospinal tract was estimated by measuring the cross-sectional area of cerebral peduncles with MRI and by calculating an index of symmetry between the two peduncles. In CH patients, a large number of parameters measured during the grip-lift task were signifi-

cantly different when compared with those found in control subjects. Among those, the duration of the pre-loading and loading phases was significantly longer in CH patients. In addition, both the dissimilarity and time-shift between the profiles of the grip and load force rates, quantified with the cross-correlation method, were also significantly larger in CH patients; the time-shift was strongly correlated with impaired dexterity. These findings suggest that impaired dextrous finger movements in CH patients may specifically result from their inability to ensure a precise synergy between fingertip forces while manipulating an object. Finally, the finding that the time-shift also correlated with the corticospinal tract dysgenesis, as estimated with the cerebral peduncle asymmetry, argues in favour of a critical role of the corticospinal system in the temporal coordination between different muscles involved in dextrous hand movements. Both digital and manual dexterity were also altered in the non-paretic hand of CH patients. This deficit may reveal the contribution of the lesioned hemisphere to the control of ipsilateral skilled finger movements.

Keywords: cerebral palsy; pyramidal tract; finger movement; grip-lift synergy

Abbreviations: CH = congenital hemiplegia; GF = grip force; LF = loading force

Introduction

Manipulating small objects, and exploring their shape and texture, require highly skilled hand and finger movements. Although the biomechanical conditions for independent finger movements are present in many primates, the neural circuitry necessary for controlling these movements is most developed in higher primates, especially in man (Nakajima

et al., 2000). A substantial amount of anatomical, electrophysiological and clinical evidence suggests that the principal constituent of the motor system underlying the performance of highly skilled finger movements is the corticospinal pathway and, more specifically, its corticomotoneuronal component (see Porter and Lemon, 1993). The portion of

the corticospinal tract originating from the primary motor cortex is largely concerned with the control of muscles acting on the wrist and fingers, and earlier studies have suggested that the primary motor cortex is necessary, and largely sufficient, to control skilled hand movements. However, recent functional imaging studies have shown that a large network including several other contralateral and ipsilateral cortical areas is also involved in the control of fine finger movements (Forssberg *et al.*, 1999; Ehrsson *et al.*, 2000, 2001). These observations suggest that, although the primary motor cortex is a prerequisite for the execution of skilled finger movements, their precise programming and control involve highly specialized brain structures.

The manipulation of small objects between the tips of the thumb and index finger requires a precise coordination between the grip force (normal to the grip surface) and load force (tangential to the grip surface). This so-called 'grip-lift synergy' is characterized by a smooth and parallel increase in both the grip and load forces, suggesting they are controlled in a predictive way (Westling and Johansson, 1984; Johansson and Westling, 1988). This anticipatory control was regarded as evidence for the existence of an internal representation of both the mechanical characteristics of the limbs and the object's physical properties in order to predict the consequences of voluntary movements; this process is thought to rely on an 'internal forward model' (Flanagan and Wing, 1997; Witney *et al.*, 2001a; Wolpert and Flanagan, 2001). After movement onset, the nervous system can optimally estimate the current state of the motor system by combining actual sensory feedback with the predictions of the forward model in order to update these internal representations (Wolpert *et al.*, 2001). Therefore, even a simple movement such as grasping and loading an object involves subtle interplay between feed-forward and feedback mechanisms in order to generate a smooth vertical acceleration of the object (Witney *et al.*, 2001b).

The complexity of the grip-lift task was further revealed by developmental studies. Before the age of two, children use a pure feedback strategy while performing a grip-lift task, as shown by multiple successive increments in both grip and load force rates (Forssberg *et al.*, 1992; Gordon *et al.*, 1992). First signs of an anticipatory control of grip and load forces appear around the age of two and develop throughout childhood to reach adult performance at the age of eight years (Forssberg *et al.*, 1991). This evolution of the grip-lift synergy parallels the development of manual skills (Forssberg *et al.*, 1991) and may reflect the protracted maturation of the corticospinal tract in primates (Olivier *et al.*, 1997; Paus *et al.*, 1999) and the progressive implementation of the cortical circuitry responsible for the control of skilled finger movements (Forssberg *et al.*, 1999; Ehrsson *et al.*, 2000, 2001).

Congenital hemiplegic (CH) patients do not usually acquire normal skilled hand movements. Although their impaired dexterity is partly due to spasticity and associated musculo-skeletal malformations, the neural control of

finger movements is known to be specifically altered in these patients (Forssberg, 1999). In CH patients, the grip-lift movement is characterized by an asynchronous onset of both grip and load forces, and by multiple successive increments in grip and load force rates (Eliasson *et al.*, 1991, 1992, 1995; Gordon and Duff, 1999a; Gordon *et al.*, 1999; Forssberg *et al.*, 1999). This pattern of movement is reminiscent of that observed in normal children younger than 2 years.

The aim of the present study was to investigate the extent to which a deficit in the coordination of fingertip forces during precision lifting could account for the impaired dexterity in CH patients. Whereas Gordon and Duff (1999b) failed to find a relationship between dexterity and performance in a grip-lift task, a correlation between a global index of grip-lift synergy and impaired dexterity in CH children was shown by Forssberg *et al.* (1999). In the current study, several individual temporal and dynamic parameters were measured during a grip-lift task in 16 CH patients and were correlated with manual and digital dexterity and with a global score of upper limb function. These results were compared with those gathered from a group of 16 age- and sex-matched control subjects. In addition, in order to investigate the specific contribution of the corticospinal pathway to skilled hand movements, both grip-lift task parameters and functional scores were correlated with the corticospinal tract dysgenesis. This was estimated by measuring the cross-sectional area of cerebral peduncles with MRI and by calculating an index of symmetry between the two peduncles. This measure proved to be a reliable index to estimate the degeneration of the corticospinal tract in CH patients (Bouza *et al.*, 1994; Staudt *et al.*, 2000).

Methods

All experimental procedures were approved by the Ethical Committee of the Université catholique de Louvain. Subjects and parents gave their written informed consent.

Subjects

Sixteen patients (age 12.6 ± 3.4 years, mean $\pm$ SD) with a congenital hemiplegia and 16 age- and sex-matched control subjects (12.8 ± 3.2 years, mean $\pm$ SD) were selected to participate in this study. A standard clinical evaluation showed hemiplegia with a predominantly upper limb distribution. The severity of the hemiplegia varied, according to Claeys *et al.* (1983), from mild, in most patients, to moderate. This was confirmed by scores on different functional tests (see below). All patients and control subjects had a normal, or nearly normal, school level for their age, suggesting that none of them had major cognitive deficits. A brief description of each patient is given in Table 1.

Table 1 Clinical description, scores on functional tests for the contralesional upper limb, lesion description and peduncular symmetry for CH patients

Patient (sex)	Age (years)	Clinical description	Pressure sensitivity (mg)	Stereognosis /10	Proprioception/5		Melbourne (%)	Lesion description (MRI)	Lesion group*	PSym (%)
					Thumb	Index				
1 (F)	8	R hemiparesis, R hand disuse	NA	4	2	3	73	L central macrocystic encephalomalacy, L ventriculomegaly, L hemispheric hypotrophy, R ventriculomegaly	1	54.7
2 (M)	8	R hemiparesis	27.5	10	5	5	99	L white matter ASI (periventricular and centrum semiovale), L ventriculomegaly, internal capsule atrophy (both ant and post limbs)	1	87.7
3 (M)	9	R hemiparesis, R hand disuse	27.5	10	5	5	55	L deep sylvian artery stroke, L ventriculomegaly	4	57.1
4 (M)	10	R hemiparesis	27.5	10	5	5	70.5	L frontal closed-lip schizencephaly, L cerebral and cerebellar hemispheric hypotrophy, mild L ventriculomegaly	1	82.7
5 (M)	10	R hemiparesis, R hand disuse	166	10	0	3	NA	L widespread cavity in frontoparietal cortex, internal capsule hypoplasia, mild L ventriculomegaly	1	61.4
6 (M)	10	R hemiparesis	27.5	10	5	5	88.5	L white matter ASI (centrum semiovale), L ventriculomegaly	3	72.4
7 (M)	11	R hemiparesis	27.5	10	5	5	96	L white matter ASI (corona radiata) consistent with remote cerebral infarction, L ventriculomegaly, R parietal microlesions	3	74.2
8 (F)	12	R hemiparesis, R hand disuse	3632	5	5	5	NA	L hemispheric atrophy with micro and macrocystic lesion in the Rolandic cortex, mild L ventriculomegaly, R discrete white matter ASI (corona radiata)	1	74.6
9 (M)	12	L hemiparesis, L hand disuse	67.7	7	2	5	51	Large R white matter ASI with R hemispheric hypotrophy	1	65.3
10 (F)	13	L mild equinus, no evident Impairment of the L upper limb	27.5	10	5	5	98	No visible lesion	0	95.2
11 (M)	13	R hemiparesis	23	10	5	5	93	L white matter ASI (corona radiata), L ventriculomegaly, small L paraventricular cyst	3	78.9
12 (F)	16	R hemiparesis	408.2	9	5	5	84	L cortico-subcortical ASI (rolandic opercule and premotor cortex lower part of the prefrontal gyrus), L hemispheric hypotrophy	2	65.4
13 (F)	16	R hemiparesis	27.5	10	5	5	98	L precentral cortico-subcortical ASI (hand knob), L paraventricular (deep parietal) ASI	3	89.1
14 (F)	17	R hemiparesis	27.5	9	5	5	100	L postcentral cortical ASI, small L posterior parietal cyst, R ventriculomegaly	2	86.5

Table 1 Continued

Patient (sex)	Age (years)	Clinical description	Pressure sensitivity (mg)	Stereognosis /10	Proprioception/5		Melbourne (%)	Lesion description (MRI)	Lesion group*	PSym (%)
					Thumb	Index				
15 (F)	17	Mild L hemiparesis with hand dyspraxia, partial seizures	27.5	10	5	5	100	R cortical cyst involving the lateral premotor cortex in front of the inferior precentral gyrus and Rolandic opercule, mild hemispheric asymmetry (R>L), L white matter ASI (parietal region and pyramidal tract in the pons)	2	92.3
16 (F)	19	L hemiparesis	23	9	5	5	89.3	R white matter ASI (deep corona radiata and central sulcus)	3	81.0

*See Methods for details. R = right; L = left; M = male; F = female; NA = not available; ASI = abnormal signal intensity; PSym = peduncular symmetry index.

MRI

Morphologic MRI were acquired for each CH patient and for 13 control subjects on a 1.5 T MRI system (Signa Horizon Echospeed, General Electric Medical Systems, Milwaukee, Wisconsin, USA) using the 3D gradient echo T₁-weighted sequence: TR (repetition time) = 23 ms; TE (echo time) = 3 ms; flip angle 30°; 124 contiguous axial slices (1.5 mm thick); FOV (field of view) = 24 cm and rectangular FOV = 75%; matrix = 256 × 256; 1 Nex. Individual MRI scans were realigned on the anterior and posterior commissural (AC–PC) plane (Talairach and Tournoux, 1988).

CH patients were classified into five groups according to the location and the extent of their lesion (see Table 1). One patient had no visible lesion on MRI (group 0). Six patients had extensive hemispheric lesions (group 1), three patients had focal cortical lesions (group 2) and five had subcortical lesions (group 3). One patient had a focal internal capsule lesion (group 4). In addition, detailed MRI analysis also showed minor lesions in the contralesional hemisphere in three patients (Patients 7, 8, 15) and ventricular dilatation in two patients (Patients 1 and 14) (see Table 1).

Upper limb assessment

Upper limb function was assessed in both CH and control subjects by means of different tests and functional scales. Both hands were systematically tested in the two groups starting with the dominant, or non-paretic, hand.

The Melbourne assessment of unilateral upper limb function is a clinical test specifically developed for children with neurological impairment (Johnson *et al.*, 1994). It consists of 16 items scored on an ordinal scale of two to four levels depending on the item; each item involved reaching, grasping, releasing or manipulating small objects. Each child was videotaped during the test performance for subsequent analysis according to the criteria described by Randall *et al.* (1999). The total raw score was expressed as a percentage of the maximal score.

Strength

The grip strength was evaluated by means of a Jamar dynamometer (Therapeutic Equipment Corporation, Clifton, New Jersey, USA) adjusted at the second smaller setting; a pinch gauge was used to measure the key pinch force (Mathiowetz *et al.*, 1986b). The tip pinch force was evaluated by means of the grip-lift apparatus (see below) (Eliasson *et al.*, 1991). The subjects were asked to squeeze the apparatus as hard as possible for 3–5 s. This method allowed us to compare the maximum tip pinch force the subject could apply on the apparatus with the static grip force. It is noteworthy that the result of this measurement is likely to be underestimated when compared with the measure proposed by Mathiowetz *et al.* (1986b). For these three strength measures, each hand was tested three times, alternately, with a rest period of 30 s in

between each trial. The final score was expressed as the mean value of the three trials.

Dexterity

The digital dexterity was measured by means of the Purdue pegboard test (Backman *et al.*, 1992; Mathiowetz *et al.*, 1986a). The score was defined as the maximum number of pegs picked up from a cup and inserted into the holes of the board, within a 30 s period of time. Each subject performed this test three times with each hand, alternating the dominant (or non-paretic) and the non-dominant (or paretic) hand. The total score was the mean value of the three trials for each hand. The manual dexterity was assessed with the box and block test (Cromwell, 1965). In this test, the score was defined as the maximum number of blocks transported individually from one compartment of a box to the other, within a 60 s period.

Pressure sensitivity

The pressure detection threshold was measured at the tip of the index finger using a Semmes-Weinstein aesthesiometer (Lafayette Instrument Company, Loughborough, UK) according to the procedure described by Bell-Krotosky (1990). This instrument consists of a set of 20 monofilaments of progressively smaller diameters, calibrated to exert a decreasing peak force when pressed and bent against the skin. With vision occluded, subjects had to report when they felt the pressure of the filament applied briefly (<1 s) perpendicularly to the finger pulp. The score was the weight (expressed in mg) required to bend the thinnest monofilament the subject could feel.

Stereognosis

Stereognosis was assessed using a version of the manual form perception test (Ayres, 1989), as modified by Cooper *et al.* (1995). Five shapes (circle, triangle, square, diamond and octagon) and five objects of daily use (toothbrush, tennis ball, comb, large cup and a sweet in wrapper) were presented to the subjects in a random order, with vision occluded. The subject was then asked to point to the object from a selection of drawings representing the ten objects. The number of objects matched correctly was taken as the stereognosis score.

Proprioception

With eyes occluded, the metacarpo-phalangeal joints of the thumb and index finger were passively moved, with a maximum of 30°. The subject was asked to identify the direction of passive joint displacements; the number of correct responses out of five trials performed for each finger was scored.

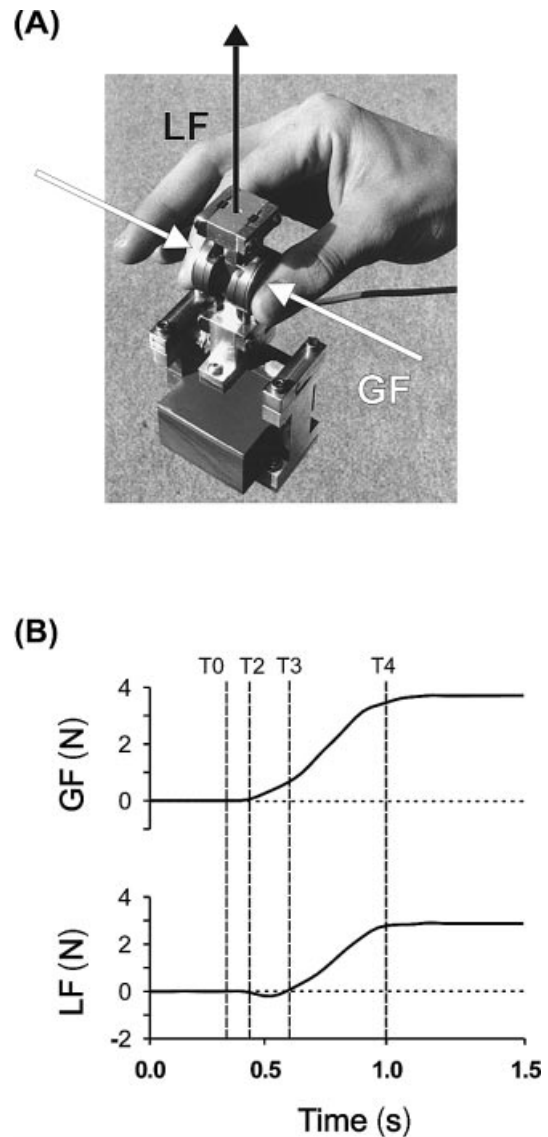


Fig. 1 (A) Apparatus used to measure the different forces during the grip-lift task. White arrows indicate the direction of the grip force (GF) (normal to the grip surface) and the black arrow shows that of the load force (LF) (tangential to the grip surface).

(B) Typical recordings of LF and the mean GF exerted by the two fingers and recorded from a normal adult subject. The vertical dotted lines indicate the different temporal parameters measured in the present study. T0–T3 = preloading phase; T2–T3 = delay between the onset of GF and LF; T3–T4 = loading phase. T0–T1 (i.e. the delay between the contact of the two fingers) is not shown since this parameter was measured on the individual traces of GF exerted by the thumb and index finger.

The grip-lift task

The apparatus used to measure fingertip forces while lifting an object was similar to that described originally by Westling and Johansson (1984) (Fig. 1A). This apparatus weighted 280 g and the two parallel vertical grip surfaces were covered with smooth brass. The force perpendicular to the grip surface (grip force, GF) and the vertical force tangential to the surface (load force, LF) were measured with strain gauge transducers.

Signals were sampled at 400 Hz with a 12-bit resolution analogue-to-digital converter (National Instruments, Austin, Texas, USA).

Subjects sat on a chair in front of a table; the chair was adjusted so that the table was just above the thighs. The task was explained carefully and demonstrated to each subject; they had a chance to practise the task a few times with each hand before data collection began. Subjects had to grasp the apparatus between the tips of the index finger and thumb, to lift it ~5 cm above the table and to maintain it in the air for ~10 s. CH patients often used an additional finger for extra support when lifting the apparatus with their paretic hand. Each subject performed 10 trials with each hand, starting always with the dominant (or non-paretic) hand. Three patients (1, 8 and 9) were unable to perform this task because their impairment was so severe they could not grasp the apparatus properly.

The following temporal parameters were measured: (i) T0–T1, the delay between the contact of the two fingers with the manipulandum; (ii) T2–T3, the delay between the onset of GF and that of LF; (iii) T0–T3, the preloading phase i.e. the delay between the contact of the first finger and the onset of LF; and (iv) T3–T4, the loading phase during which both GF and LF increase until LF becomes equal to the weight of the object (see Fig. 1B).

The loading phase is followed by a static phase, during which the object is held stationary.

We also measured the following dynamic parameters: (i) the first derivative of both LF and GF i.e. the grip force rate (dGF/dt) and load force rate (dLF/dt); (ii) the peak GF i.e. the maximal value of GF reached during the loading phase; (iii) the value of GF at LF onset (i.e. at T3) expressed as a percentage of peak GF; (iv) the static GF expressed with respect to the static LF (GF/LF); and (v) the average value of dGF/dt calculated between the onset and the peak of GF.

The precise synergy between GF and LF was assessed by computing, for each trial, a cross-correlation function between dLF/dt and dGF/dt. This method consists in searching for the larger coefficient of correlation between the two signals by shifting one signal with respect to the other one in order to cancel out the effect of a possible asynchrony. In the example illustrated in Fig. 2A, both dLF/dt and dGF/dt had a very similar profile but were slightly asynchronous and the maximum correlation was searched by systematically shifting, by steps of 2.5 ms, dGF/dt with respect to dLF/dt (Fig. 2B). In this example, the shift of dGF/dt required to maximize the coefficient of correlation was 20 ms, indicating that GF increase led LF increase. Therefore, for each trial, this method provides us with two values: the maximum coefficient of correlation, which indicates the similarity between the profiles of the two force rates, and the time-shift, which provides an objective measure of the asynchrony between dGF/dt and dLF/dt. A positive value for the time-shift indicates that GF leads LF, whereas a negative time-shift value indicates that GF lags LF. We also computed the

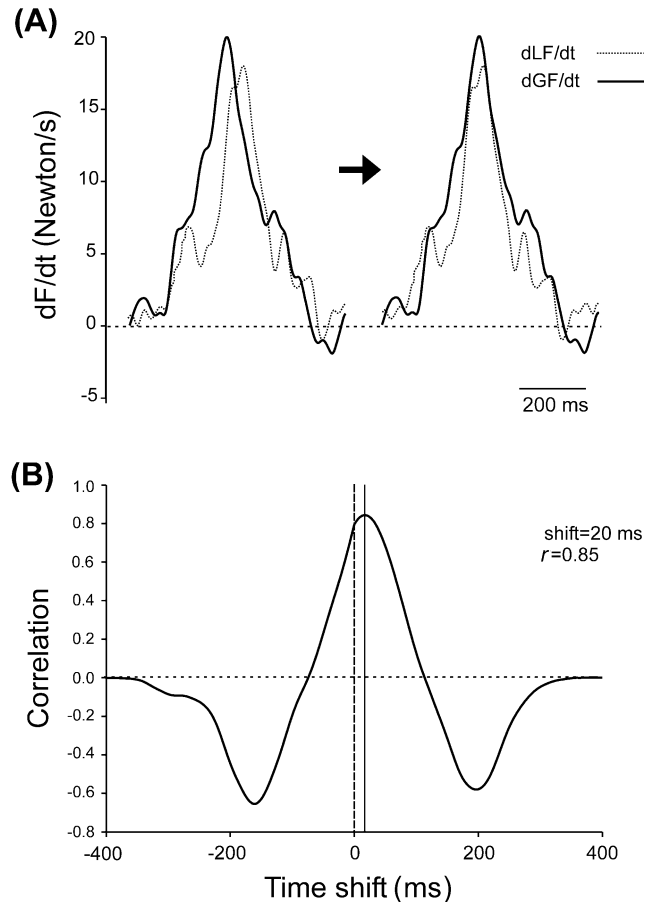


Fig. 2 Cross-correlation method. (A) Profiles of dGF/dt and dLF/dt before (left) and after (right) they were shifted by the value given by the cross-correlation function. (B) Example of a cross-correlation function computed between dGF/dt and dLF/dt. This method consists of searching for the larger coefficient of correlation between the two signals by shifting dGF/dt with respect to dLF/dt, by a step of 2.5 ms. In this particular example, the shift of dGF/dt necessary to maximize the coefficient of correlation was 20 ms; after this manoeuvre, the correlation between dGF/dt and dLF/dt was 0.85. The vertical dashed line indicates the zero lag position.

absolute value of this time-shift to obtain a global estimate of the asynchrony between the two force rates.

Index of peduncular symmetry

Cross-sectional area of the cerebral peduncles in the mesencephalon was measured in order to estimate the dysgenesis of the corticofugal pathways (Bouza *et al.*, 1994; Staudt *et al.*, 2000). The area of the left and right cerebral peduncles was measured in a transverse plane passing through the mammillary bodies, five or six slices below the AC–PC plane. Because it was not always possible to dissociate the substantia nigra from the cerebral peduncles, the substantia nigra was also included in our measurements (see Fig. 6). In 15 CH patients, the absolute value of the peduncle area was expressed in mm²; in one CH patient,

Table 2 Dexterity and strength in CH patients and control subjects

Tests	CTRL _{ndom} Mean (SD)	CTRL _{dom} Mean (SD)	<i>P</i> value (CTRL _{ndom} / CTRL _{dom})	CH _{paretic} Mean (SD)	<i>P</i> value (CTRL _{ndom} / CH _{paretic})	CH _{non-par} Mean (SD)	<i>P</i> value (CTRL _{dom} / CH _{non-par})
Digital dexterity (n)	15 (1.5)	16 (1.3)	0.005*	5 (4.7)	<0.001*	14 (2.1)	<0.001*
Manual dexterity (n)	69 (7.6)	71 (8.2)	0.21	36 (17.1)	<0.001*	55 (11.8)	0.001*
Grip strength (newtons)	240 (73.8)	255 (85.2)	0.031	108 (93.8)	<0.001*	196 (82.9)	0.004*
Key pinch force (newtons)	65 (15.6)	68 (15.4)	0.12	42 (17.7)	<0.001*	68 (15.0)	0.85
Tip pinch force (newtons)	36 (9.9)	40 (13.4)	0.004*	24 (9.6)	<0.001*	40 (15.8)	1.00

* $P \leq 0.005$; CTRL_{ndom} = non-dominant hand of control subjects; CTRL_{dom} = dominant hand of control subjects; CH_{paretic} = paretic hand of CH patients; CH_{non-par} = non-paretic hand of CH patients.

the peduncular area was only available as a pixel number. The index of symmetry was defined as follows: (ipsilesional peduncular area/contralesional peduncular area) $\times$ 100%. In 13 out of 16 control subjects, the index of symmetry was defined as follows: (non-dominant side peduncular area/dominant side peduncular area) $\times$ 100%.

Statistics

Paired *t*-tests were used to compare: (i) the performance of both hands in control subjects and CH patients; and (ii) the performance of the paretic and non-paretic hands of each CH patients with the non-dominant and dominant hands, respectively, of his/her age-matched control. Non-parametric statistics were applied when normality test failed (Kolmogorov-Smirnov, $P < 0.001$) or when statistics were performed on ordinal-level data. Hence, a Friedman repeated measure analysis of variance on ranks was performed in control subjects and CH patients to search for a possible effect of repetition over the ten trials of the grip-lift task. A Spearman rank order correlation was used to determine the correlation between the grip-lift parameters, the upper limb function, the index of peduncular symmetry and the location, or the existence, of a lesion on any side. Given the large number of tests, the level of significance for the *P* value was set to 0.005 in order to minimize type 1 statistical errors.

Results

Upper limb assessment

The scores of CH patients on the functional and clinical tests performed on the paretic hand are listed in Table 1. Four patients had a deficit in pressure sensitivity (>67.7 mg) and three in proprioception; a deficit in stereognosis was found in six patients. When the non-paretic hand was assessed, all CH patients had a maximal score on all these tests, except for Patients 1 and 12, who had a deficit in pressure sensitivity. The scores of CH patients on the Melbourne test ranged from 51 to 100%; two patients (14 and 15) and all control subjects had a maximum score on this test (see Table 1).

Table 2 presents the results of dexterity and strength tests performed in both CH patients and control subjects. In control

subjects, the score on the Purdue pegboard test revealed a better digital dexterity in the dominant hand (CTRL_{dom}) than in the non-dominant hand (CTRL_{ndom}) ($t = 3.295$, $P = 0.005$). The fingertip strength was also significantly larger in the dominant hand than in the non-dominant hand of control subjects ($t = 3.381$, $P = 0.004$).

In CH patients, as expected, the results of dexterity and strength tests disclosed a statistically significant difference between the paretic (CH_{paretic}) and non-paretic hand (CH_{non-par}) ($P < 0.001$ in all five tests; not shown in Table 2). When the paretic hand of CH patients was compared with the non-dominant hand of control subjects, both the dexterity and strength were significantly reduced in patients ($P < 0.001$ on all five tests). CH patients also showed a worse digital ($t = -5.41$, $P < 0.001$) and manual ($t = -7.76$, $P = 0.001$) dexterity when their non-paretic hand was compared with the dominant hand of control subjects; they also had a lower grip strength ($t = -3.4$, $P = 0.004$) (see Table 2).

The grip-lift task

The performance of CH patients in the grip-lift task was strikingly different from that observed in control subjects. As shown in the example illustrated in Fig. 3B for a CH patient, the preloading phase (i.e. the delay before LF started to increase, T0–T3) was much longer than in the control subject. Then, both GF and LF increased in a less synchronous and less harmonious manner, as indicated by the noisier profiles of GF and LF rates. Altogether, this led to an overall increase in the duration of the initial phases of the grip-lift task in CH patients when compared with controls. This strategy contrasts with that observed in control subjects, namely a nearly simultaneous onset and parallel increase of GF and LF and a synchronous occurrence of the peaks of GF rate and LF rate, by the middle of the loading phase (T3–T4) (Fig. 3A).

The difference between the performance of CH patients and controls in the grip-lift task was further evidenced by the cross-correlation method. As shown in Fig. 3C, in the control subject, the correlation between dGF/dt and dLF/dt was rather high, attesting a close similarity between the profiles of GF

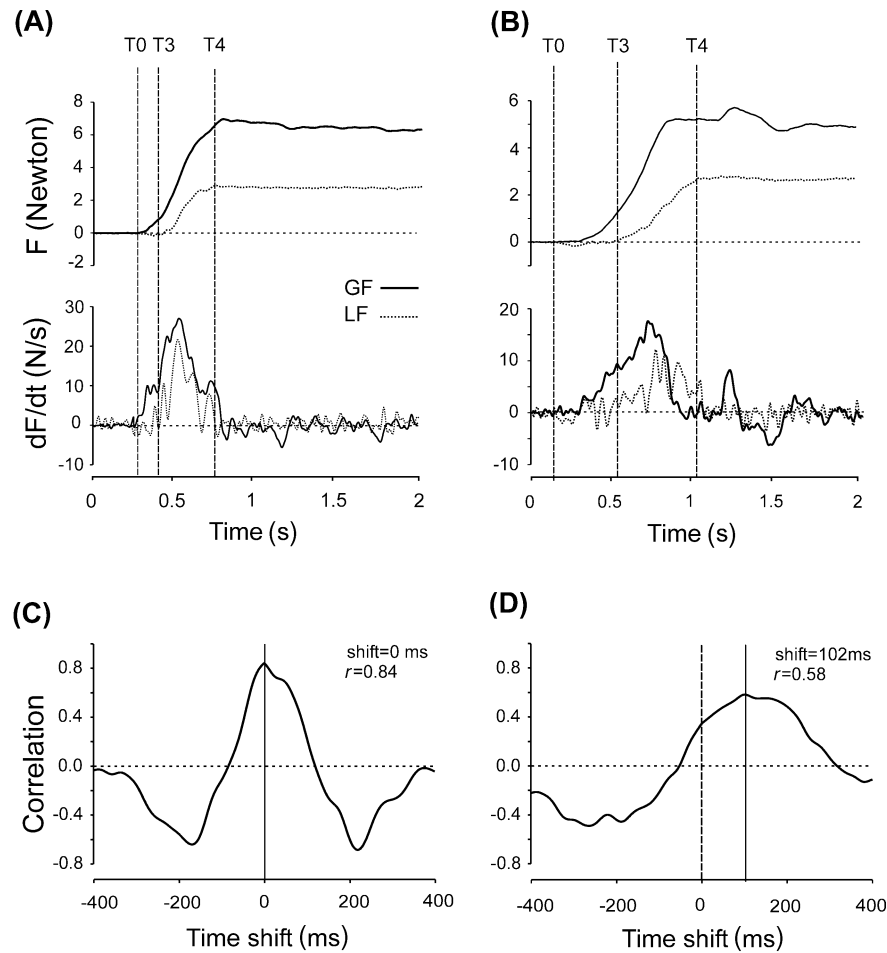


Fig. 3 Fingertip forces and cross-correlation functions found in a 16-year-old CH patient (13) (right) and her matched control subject (left). (A–B) The grip force (GF), load force (LF), grip force and load force rate profiles (dF/dt) recorded during the grip-lift task are plotted as a function of time. The vertical dashed lines indicate different temporal parameters analysed. T0–T3 = preloading phase; T3–T4 = loading phase. (C) Cross-correlation function computed in the control subject; the maximum of the cross-correlation function ($r = 0.84$) was found for the zero time lag position. (D) Cross-correlation function calculated in the CH patient; the maximum of the cross-correlation was much lower ($r = 0.58$) and was obtained after dGF/dt was shifted by 102 ms.

and LF rates. In addition, the finding that this correlation was found for a 0 ms time-shift proved that, in this example, both GF and LF increased synchronously. In contrast, in the CH patient we found both a lower correlation between GF and LF rates and a longer time-shift that indicate, respectively, the dissimilarity and the asynchrony between GF and LF rates (Fig. 3D). In this particular example, the peak of GF rate led that of LF by 102 ms.

These results were representative of those found for the whole population of patients and controls. As shown in Fig. 4A and B, the time-shift found in controls was shorter (median: 15 ms) than in CH patients (median: 35 ms). Moreover, although the dispersion of time-shift values in controls was far from being negligible, the time-shift distribution in CH patients was found much wider, ranging between ~ 20 ms and ~ 200 ms (Fig. 4A). In both groups, only

a few cases of negative time-shift values were found. The mean time-shift was not statistically different in CH patients (54 ± 44.4 ms, mean $\pm$ SD) when compared with controls (23 ± 15.4 ms) ($t = 2.43$; $P = 0.032$); however, when the absolute value of the time-shift was computed, it showed a significant difference between patients (72 ± 39.1 ms) and controls (29 ± 13.1 ms) ($t = 3.48$; $P = 0.005$) (see Table 3). The distributions of correlation values gathered in CH patients (Fig. 4C) and in control (Fig. 4D) were also clearly dissimilar. We found a significantly lower correlation between the first derivatives of GF and LF in the paretic hand of CH patients (0.56 ± 0.14 , mean $\pm$ SD) than in the non-dominant hand of controls (0.71 ± 0.10) ($t = -3.74$; $P = 0.003$). These observations further support our conclusion that the synergy between LF and GF was specifically impaired in CH patients.

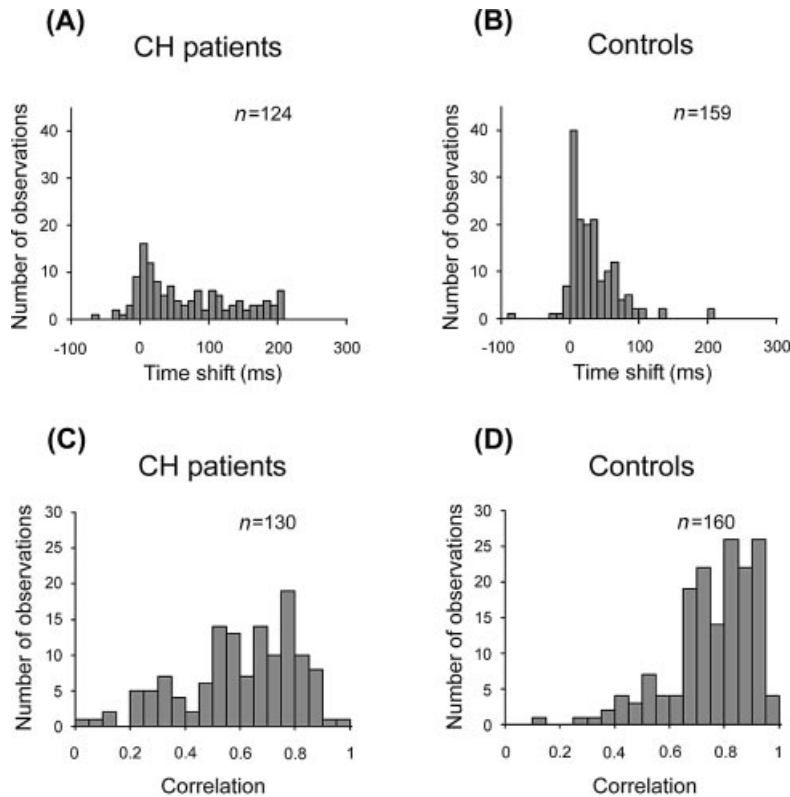


Fig. 4 Results of the cross-correlation analysis computed on individual trials of CH patients ($n = 13$) and of controls ($n = 16$); this calculation was performed separately for each trial ($n = 10$) performed by subjects. (A–B) Distribution of the time-shift values calculated for the paretic hand of CH patients (A) and the non-dominant hand of the control subjects (B). Six extreme negative values in CH patients and one in controls are not represented. (C–D) Distribution of the r values computed for the paretic hand of CH patients (C) and the non-dominant hand of the control subjects (D).

Table 3 Grip-lift parameters in CH patients and control subjects

Parameters	CTRL _{ndom} Mean (SD)	CTRL _{dom} Mean (SD)	P value (CTRL _{ndom} / CTRL _{dom})	CH _{paretic} Mean (SD)	P value (CTRL _{ndom} / CH _{paretic})	CH _{non-par} Mean (SD)	P value (CTRL _{dom} / CH _{non-par})
Delay thumb–index, T0–T1 (ms)	62 (22.7)	58 (29.9)	0.62	127 (87.1)	0.026	81 (22.4)	<0.001*
GF _{onset} –LF _{onset} , T2–T3 (ms)	95 (51.7)	97 (36.1)	0.90	294 (161.6)	<0.001*	116 (58.1)	0.35
Preloading, T0–T3 (ms)	174 (75.9)	178 (54.5)	0.77	544 (371.7)	0.003*	227 (52.8)	0.03
Loading, T3–T4 (ms)	269 (77.5)	296 (107.3)	0.11	492 (119.4)	<0.001*	389 (117.7)	0.07
GF at LF>0 (%)	16 (7.1)	18 (9.8)	0.34	28 (18.3)	0.046	14 (6.9)	0.31
Mean GFr (newton/s)	9 (3.9)	10 (7.3)	0.40	5 (2.2)	0.009	7 (3.0)	0.23
GF/LF	1.0 (0.3)	1.1 (0.4)	0.08	1.6 (0.6)	0.05	1.4 (0.8)	0.23
Cross-correlation	0.71 (0.1)	0.73 (0.1)	0.35	0.56 (0.14)	0.003*	0.69 (0.05)	0.14
Abs-shift (ms)	29 (13.1)	24 (16.3)	0.46	72 (39.1)	0.005*	28 (11.5)	0.51

* $P \leq 0.005$; CTRL_{ndom} = non-dominant hand of control subjects; CTRL_{dom} = dominant hand of control subjects; CH_{paretic} = paretic hand of CH patients; CH_{non-par} = non-paretic hand of CH patients; Delay thumb–index, T0–T1 = delay between the contact of the thumb and index finger; GF_{onset}–LF_{onset}, T2–T3 = delay between the grip force (GF) onset and load force (LF) onset; Preloading (T0–T3) = preloading phase; Loading, T3–T4 = loading phase; GF at LF>0 = GF at LF onset (T3), expressed in percentage of the peak GF; Mean GFr = mean GF rate; Cross-correlation = r value obtained by the cross-correlation method (see Methods); Abs-shift = absolute value of the shift obtained by the cross-correlation method (see Methods).

Table 3 gives the mean values of the different temporal and dynamic parameters measured during the grip-lift task for the whole population of CH patients and control subjects. In

control subjects, the performance of the non-dominant hand was indistinguishable from that of the dominant hand during the grip-lift task. In contrast, as expected, a significant

Table 4 Correlation coefficients (*r*) between the grip-lift parameters and upper limb motor function

	Grip-lift parameters								
	Delay thumb-index (T0–T1)	GF _{onset} –LF _{onset} (T2–T3)	Preloading (T0–T3)	Loading (T3–T4)	GF at LF>0	Mean GFr	GF/LF	Cross-corr	Abs-shift
Melbourne	–0.68	–0.63	–0.82*	–0.41	–0.66	0.43	0.42	0.50	–0.61
Digital dexterity†	–0.58	–0.58	–0.89*	–0.48	–0.69	0.65	0.62	0.60	–0.77*
Manual dexterity‡	–0.36	–0.55	–0.79*	–0.69	–0.50	0.68	0.46	0.56	–0.58

* $P < 0.001$; †As measured by the Purdue pegboard test. ‡As measured by the box and block test. Delay thumb-index (T0–T1) = delay between the contact of the thumb and index finger on the apparatus; GF_{onset}–LF_{onset} (T2–T3) = delay between the grip force (GF) onset and load force (LF) onset; Preloading (T0–T3) = preloading phase; Loading (T3–T4) = loading phase; GF at LF>0 = GF at LF onset (T3), expressed in percentage of the peak GF; Mean GFr = mean GF rate (see Methods); Cross-corr = maximum *r* value obtained by the cross-correlation method (see Methods); Abs-shift = absolute value of the shift obtained by the cross-correlation method (see Methods).

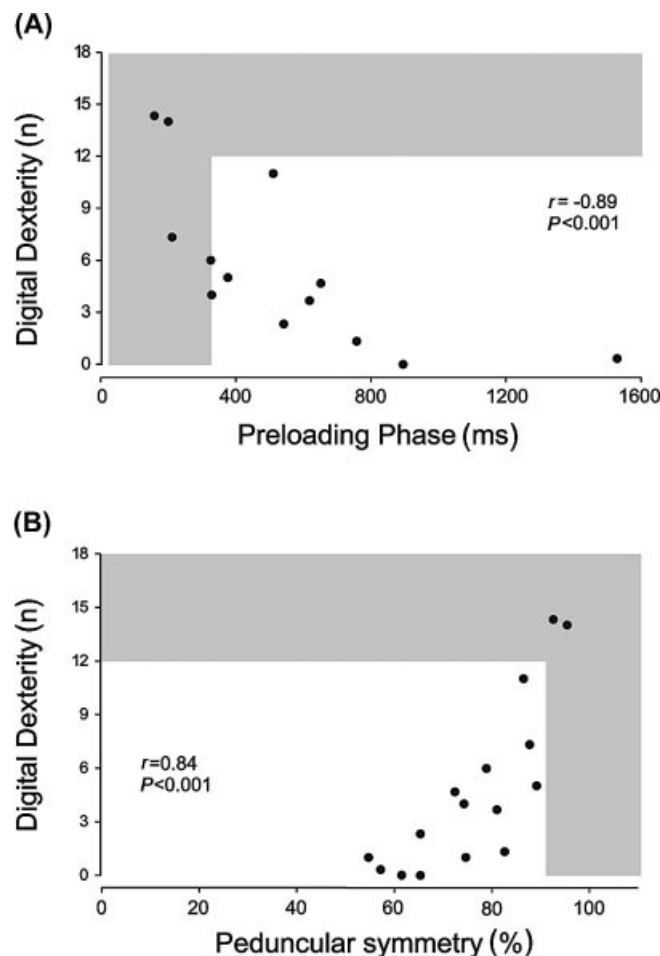


Fig. 5 (A) Correlation between the preloading phase duration and digital dexterity of the paretic hand of 13 CH patients as measured by the Purdue pegboard test. The grey shaded areas indicate the range of normal value (mean $\pm$ 2 SD) measured in the non-dominant hand of control subjects ($n = 16$) for both the preloading phase duration (174 ± 152 ms) and the dexterity (15 ± 3). (B) Correlation between the corticospinal tract dysgenesis in CH patients, as estimated with the index of peduncular symmetry, and the digital dexterity of their paretic hand, as measured by the Purdue pegboard test ($n = 16$). The grey shaded areas indicate the range of normal value (mean $\pm$ 2 SD) measured in control subjects for both the index of peduncular symmetry ($101 \pm 10.4\%$, $n = 13$) and the dexterity (15 ± 3).

difference was observed between a large number of grip-lift parameters when the paretic hand of CH patients was compared with the non-dominant hand of control subjects. Both the preloading and loading phases were significantly longer in CH patients (see Table 3). Within the preloading phase, the delay between the onset of GF and LF (T2–T3) was significantly prolonged whereas the delay between the contact of the two fingers with the object (T0–T1), although longer in CH patients, did not reach the significance level. There was a clear trend for a higher value of GF at LF onset and for a lower mean GF rate in CH patients, but these differences were not statistically significant. When the non-paretic hand of the CH patients was compared with the dominant hand of the control subjects, the delay between the thumb and index finger contact (T0–T1) was also found longer in CH patients (see Table 3), suggesting that the non-paretic hand was also somewhat impaired.

In both control subjects and CH patients, the Friedman repeated measure analysis of variance on ranks failed to disclose an influence of repetition on parameters measured during the grip-lift task.

Correlation between the grip-lift parameters and dexterity

There was a significant negative correlation between the preloading phase duration and digital and manual dexterity and the Melbourne score (see Table 4); the negative correlation between the preloading phase duration and digital dexterity ($r = -0.89$, $P < 0.001$) is illustrated in Fig. 5A. The digital dexterity also correlated significantly with the absolute value of the time-shift between GF and LF rate ($r = -0.77$, $P < 0.001$). None of the dynamic grip-lift parameters correlated with the dexterity or the Melbourne score.

Index of peduncular symmetry

As illustrated in Fig. 6, one consistent feature of CH patients was a distinct peduncular asymmetry (see Table 1 for individual values in CH patients). On average, in CH patients, the area of the ipsilesional peduncle was 137.6 ± 27.2 mm²

(mean $\pm$ SD, $n = 15$); it was significantly smaller than the peduncular area measured on the non-dominant side in controls ($180.5 \pm 17.8 \text{ mm}^2$, $n = 13$) ($t = 4.04$, $P = 0.002$). In contrast, the area of the contralesional peduncle in patients ($181.7 \pm 18.6 \text{ mm}^2$, $n = 15$) was not significantly different from the peduncular area measured on the dominant side in control subjects ($179.4 \pm 22.5 \text{ mm}^2$, $n = 13$) ($t = 0.167$, $P = 0.871$).

In CH patients, the area of the ipsilesional peduncle (mean $\pm$ SD: $137.6 \pm 27.2 \text{ mm}^2$, $n = 15$) was significantly smaller than that of the contralesional peduncle ($181.7 \pm 18.6 \text{ mm}^2$, $n = 15$) ($t = 7.054$, $P < 0.001$). It is interesting to note that the cross-sectional area of the contralesional peduncle in CH patients was identical to values found in controls. The index of peduncular symmetry in patients ranged from 54.7 to 95.3% (mean $\pm$ SD: $76.2 \pm 12.6\%$, $n = 16$) (see Table 1). In control subjects, the index of peduncular symmetry varied between 91.3% and 109.2% (mean $\pm$ SD: $100.8 \pm 5.1\%$, $n = 13$).

Correlation between the dexterity and the peduncular symmetry

The index of peduncular symmetry was highly correlated with the Melbourne score ($r = 0.81$) and with both manual

($r = 0.86$) and digital dexterity ($r = 0.84$; $P < 0.001$ for all tests); the correlation between the digital dexterity and the index of peduncular symmetry is illustrated in Fig. 5B. The index of peduncular symmetry was also found to be negatively correlated with preloading phase duration ($r = -0.76$, $P < 0.001$), the GF at LF onset ($r = -0.64$, $P = 0.005$) and the absolute time-shift value ($r = -0.71$, $P = 0.005$).

No correlation was found between the anatomical location of the lesion (see Methods), and grip-lift synergy and functional parameters for the paretic hand. In the non-paretic hand, no correlation was found between the motor deficits, the presence of a minor lesion in the undamaged hemisphere (Patients 1, 7, 8, 14, 15) and the index of peduncular symmetry.

Discussion

Deficits in dextrous finger movements, which require accurate opposition of the thumb and index finger, were investigated in CH patients by quantifying the scaling and coordination of fingertip forces while lifting an object. This so-called 'grip-lift task' has proved to be very sensitive to reveal subtle deficits in skilled hand movements (Eliasson *et al.*, 1991; Forssberg *et al.*, 1999, 2000; Pereira *et al.*, 2001).

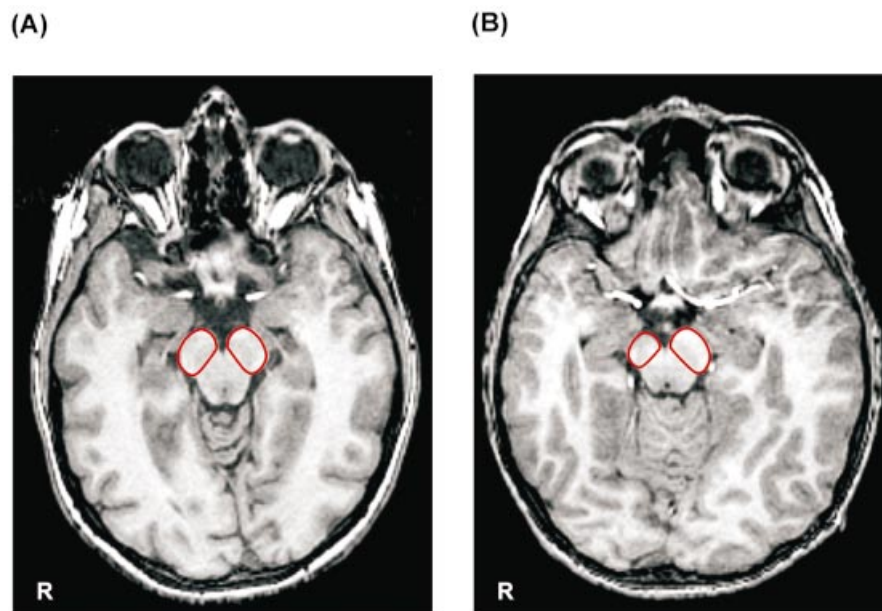


Fig. 6 Axial ($-10 \text{ mm AC-PC plane}$) T_1 -weighted MRI at the level of mesencephalon showing the cerebral peduncles (CP) in one CH and one control subject. Cross-sectional area of the left and right CP was measured in a transverse plane passing through the mammillary bodies and because of the difficulty to dissociate the substantia nigra from the cerebral peduncles; it was also included in our measurements. An index of peduncular symmetry was used to quantify dysgenesis and/or degeneration of the corticospinal tract. (A) Symmetry between the right (194 mm^2) and left (193 mm^2) cerebral peduncles in a control subject (Subject 16); in this subject, the index of peduncular symmetry equals 101%. (B) In Patient 9, with a large right matter infarct, cerebral peduncles were clearly asymmetrical. The cross-sectional area of the right and left peduncles was 115 mm^2 and 176 mm^2 , respectively; the index of symmetry was 65% and was associated with severe motor deficits.

This approach provides further insight into the mechanisms responsible for motor deficits of the hand and a better understanding of the computational principles underlying motor control (Flanagan and Wing, 1997; Wolpert and Flanagan, 2001).

Deficit in grip-lift movements in CH patients

Earlier studies have shown that CH patients have a distinct deficit in scaling and coordinating fingertip forces while lifting an object between the thumb and index finger (Eliasson *et al.*, 1991, 1992, 1995; Gordon and Duff, 1999a; Forssberg *et al.*, 1999). The present study both supports and extends these results with the finding that mainly temporal parameters of the grip-lift task were altered in CH patients.

In agreement with previous studies (Eliasson *et al.*, 1991, 1992, 1995; Gordon and Duff, 1999a), we found a significant increase in the duration of both the preloading (T0–T3) and loading phases (T3–T4) in CH patients. A longer preloading phase in patients could, at least partly, be explained by a significant increase of the T2–T3 delay (i.e. the delay between the onset of GF and LF). This observation confirms that, in CH patients, GF and LF increase in a more serial manner than in controls (Eliasson *et al.*, 1991). The asynchrony between GF and LF increase was further investigated by computing the cross-correlation function between the first derivatives of GF and LF; this method provided us with a reliable measurement of the time-shift between both force rates. Interestingly, even in control subjects, the time-shift between GF and LF was far from being negligible and ranged between about –10 to 50 ms, indicating that GF and LF rates were not absolutely synchronous. In CH patients, the time-shift was found significantly longer and more widely distributed than in control subjects, confirming the inability of CH patients to ensure a precise synergy between fingertip forces while manipulating an object.

In addition to a larger asynchrony between GF and LF rates, profiles of both force rates were found more dissimilar in CH patients than in controls. Indeed, even when the GF rate profile was realigned with the LF rate profile in order to compensate for the time-shift, the coefficient of correlation remained, on average, significantly smaller in patients than in control subjects. This confirms the finding that in CH patients one consistent feature of grip-lift movements is the large number of small irregular increments in grip and load force rates (Eliasson *et al.*, 1991) that contrast with the unimodal and smooth bell-shaped profiles of GF and LF rates found in control subjects (Johansson and Westling, 1988; Forssberg *et al.*, 1991). This measurement is the first attempt to quantify the degree of dissimilarity between both grip and load force rates found in CH patients. In CH patients, these multi-peaked GF and LF rates may reflect the use of a probing strategy comparable to that described in very young children (Forssberg *et al.*, 1991) and in adults who lack confidence about object's physical properties (Gordon *et al.*, 1993). However, it cannot be excluded that other factors such as co-

contraction (Gibbs *et al.*, 1999) or spasticity had a negative influence on this correlation.

In normal subjects, the finding that force rate profiles are synchronous and unimodal has been regarded as evidence for an anticipatory scaling of force output (Forssberg *et al.*, 1991, 1992; Gordon, 1992; Gordon *et al.*, 1992). The current results confirm that CH patients lack this ability to programme the different components of grip-lift movements in advance and that they are unable to ensure a precise temporal coordination between the different muscles involved in dextrous hand movements.

Correlation between the grip-lift parameters and dexterity

A correlation between a global index of grip-lift synergy and impaired dexterity has already been shown in CH patients by Forssberg *et al.* (1999); however, a correlation between individual grip-lift parameters and dexterity has never been reported. In the present study, we found that, in CH patients, the preloading phase duration was significantly correlated with manual and digital dexterity but also with the score on the Melbourne test. These correlations are difficult to interpret because the preloading phase consists of a large number of different processes taking place successively (Steenbergen *et al.*, 1998). However, the time-shift between the profile of GF and LF rates was found correlated with digital dexterity. This further emphasizes that a tight temporal relationship between fingertip forces is of critical importance when manipulating small objects between the thumb and index finger, and that altering this synergy may dramatically impair dextrous finger movements. On the other hand, the absence of correlation between dexterity and GF and LF rate correlation suggests that, in CH patients, the presence of multiple irregular increments in both grip and load force rates is not synonymous with a poorer performance in skilled finger movements.

Peduncular asymmetry and impaired dexterity in CH patients

The present study confirms that most CH patients had a significant asymmetry of the cerebral peduncles when compared with control subjects (Bouza *et al.*, 1994; Niemann *et al.*, 1996; Staudt *et al.*, 2000); similar findings have been reported in adult stroke patients (Fukui *et al.*, 1994). Although several other corticofugal pathways are included in this measurement (Lemon, 1999), the asymmetry of the brainstem, or peduncle, has been regarded as a reliable estimate of the corticospinal tract degeneration (Bouza *et al.*, 1994; Staudt *et al.*, 2000). It is noteworthy that, in the present study, the cross-sectional area of the contralesional peduncle in CH patients was found identical to that of age-matched controls; therefore, the smaller index of peduncular symmetry found in CH patients was exclusively due to an atrophy of the

damaged corticospinal tract and not to a compensatory overgrowing of the undamaged corticospinal tract. This observation indicates that, although transcranial magnetic stimulation studies have suggested that, after early brain injury, the contralesional corticospinal tract may play a crucial role in motor recovery (Carr *et al.*, 1993; Vandermeeren *et al.*, 2002b), it does not result in macroscopically visible structural changes. This is in agreement with studies in monkeys showing that an early unilateral section of the corticospinal tract at birth does not yield a demonstrable structural reorganization of the corticospinal projections originating from the undamaged hemisphere (Galea and Darian-Smith, 1997a).

The present study confirmed the relationship between the degeneration of corticospinal tract and the severity of motor deficits (Bouza *et al.*, 1994; Fukui *et al.*, 1994; Sawlani *et al.*, 1997), although this view has been questioned in adult stroke patients (Miyai *et al.*, 1998). We further extended these previous results with the finding that the peduncular asymmetry correlated strongly with the deficits in dextrous finger movements found in CH patients. This observation is in agreement with results from monkey experiments showing that, after an early lesion of the corticospinal tract, although a remarkable recovery of manual dexterity may be observed, dextrous movements essential to grasp a small piece of food between the thumb and index finger remained irremediably impaired (Passingham *et al.*, 1983; Galea and Darian-Smith, 1997b; Rouiller *et al.*, 1998). In CH patients, a correlation between the grip-lift synergy and the structural damage of the brain, as estimated by measuring the total lesion extent in the damaged hemisphere, has already been reported by Forssberg *et al.* (1999). However, as repeatedly observed, the correlation between the lesion extent and functional outcome is usually rather poor or even absent (Bouza *et al.*, 1994; Staudt *et al.*, 2000); the measure of the brainstem asymmetry is probably a more reliable index because it provides an estimate of the corticospinal damage consequent on the lesion, irrespective of its size or location. In addition, because it is possible to evidence an asymmetry of the brainstem as early as 3 months after birth (Bouza *et al.*, 1994; Pennock *et al.*, 1993), i.e. much before deficits in skilled hand movements become evident clinically, this index also has a distinct prognostic relevance.

The correlation between such a global estimate of the corticospinal tract degeneration and rather subtle deficits in motor programming evidenced by the grip-lift task may appear somewhat puzzling. It is, however, important to keep in mind that, in addition to the primary motor cortex, a large number of cortical areas contribute efferent axons to the corticospinal track (He *et al.*, 1993, 1995; Galea and Darian-Smith, 1994) and that recent functional MRI studies have suggested that the control of the precision grip is distributed among the same network of cortical areas (Ehrsson *et al.*, 2000, 2001; Kuhtz-Buschbeck *et al.*, 2001). The peduncular asymmetry may therefore reflect the extent to which the development of these different cortical areas was affected by

an early lesion (Marin-Padilla, 1997; Vandermeeren *et al.*, 2002a); the correlation between dexterity and peduncular asymmetry further supports the distributed nature of the control of the precise coordination of fingertip forces (Lemon, 1999; Ehrsson *et al.*, 2000, 2001; Kuhtz-Buschbeck *et al.*, 2001). Alternatively, it may be argued that the peduncular symmetry index reflects mainly the damage of larger corticospinal axons originating from the primary motor cortex.

Deficits in the non-paretic hand

In agreement with previous studies, we found that the non-paretic hand of CH patients also shows some discrete motor impairments (Gordon *et al.*, 1999; Mercuri *et al.*, 1999); similar results have been reported in adult stroke patients (Jones *et al.*, 1989; Thilmann *et al.*, 1990; Marque *et al.*, 1997; Debaere *et al.*, 2001). In the present study, we found a significant deficit in the digital and manual dexterity in the non-paretic hand of CH patients when compared with the non-dominant hand of controls. However, it is noteworthy that, except for T0–T1, the grip-lift task failed to disclose a significant difference between the performance of controls and that of CH patients when they used their non-paretic hand. This may question the sensitivity of the grip-lift task to detect subtle motor deficits. However, it may be argued that the two tests we used to assess digital and manual dexterity are more complex than the grip-lift task because they comprise other movement components such as the preshaping of the hand (Jeannerod *et al.*, 1995) and the precise manipulation of the objects. It is probable that, at least in some patients, these components were affected leading to a lower score on these two tasks.

Mercuri *et al.* (1999) suggested that an impairment of the non-paretic hand invariably reveals the existence of a discrete lesion involving the contralesional hemisphere. In the present study, although detailed MRI analysis showed discrete lesions to the contralesional hemisphere in three patients and a ventricular dilatation in two others, those subjects did not have more severe deficits in the non-paretic hand than the other patients; contralesional lesions are therefore unlikely to explain the impairment observed in the ipsilesional hand of all CH patients. Recent functional imagery studies have stressed the important contribution of the ipsilateral motor areas during precision grip tasks, particularly when the demand on dextrous control increases i.e. when the task becomes more difficult (Ehrsson 2000, 2001; Kuhtz-Buschbeck *et al.*, 2001). The motor deficit observed in the non-paretic hand of CH patients may, therefore, reveal the loss of the contribution of the damaged hemisphere to the control of the non-paretic, ipsilateral hand movements.

Acknowledgements

We wish to thank A. Smith for his comments on an earlier version of this manuscript. Thanks are also due to A. De

Volder and A. S. Augurelle for their help with data collection. We are also grateful to O. White and M. Penta for their help with data analysis. J.D. is a research assistant at the Belgian National Funds for Scientific Research (FNRS). This work was supported by a grant from the Fonds de la Recherche Scientifique Médicale (FRSM 3.4549.99) and internal grants from the Université catholique de Louvain (FSR).

References

- Ayres AJ. Sensory integration and praxis test. Los Angeles: Western Psychological Services; 1989.
- Backman C, Cork S, Gibson D, Parson J. Assessment of hand function: the relation between pegboard dexterity and applied dexterity. *Can J Occup Ther* 1992; 59: 208–13.
- Bouza H, Dubowitz LM, Rutherford M, Pennock JM. Prediction of outcome in children with congenital hemiplegia: a magnetic resonance imaging study. *Neuropediatrics* 1994; 25: 60–6.
- Bell-Krotosky J. Light touch-deep pressure testing using Semmes-Weinstein monofilaments. In: Hunter JM, Schneider LH, Mackin EM, Callahan AD, editors. *Rehabilitation of the hand*. 3rd ed. St Louis (MO): Mosby; 1990. p. 585–93.
- Carr LJ, Harrison LM, Evans AL, Stephens AJ. Patterns of central motor reorganization in hemiplegic cerebral palsy. *Brain* 1993; 116: 1223–47.
- Claeys V, Deonna T, Chrzanowski R. Congenital hemiparesis: the spectrum of lesions. *Helv Paediatr Acta* 1983; 38: 439–55.
- Cooper J, Majnemer A, Rosenblatt B, Birnbaum R. The determination of sensory deficits in children with hemiplegic cerebral palsy. *J Child Neurol* 1995; 10: 300–9.
- Cromwell FS. Occupational therapists manual for basic skills assessment: primary prevocational evaluation. Pasadena (CA): Fair Oaks Printing; 1965.
- Debaere F, Van Assche D, Kiekens C, Verschueren SM, Swinnen SP. Coordination of upper and lower limb segments: deficits on the ipsilesional side after unilateral stroke. *Exp Brain Res* 2001; 141: 519–29.
- Ehrsson HH, Fagergren A, Jonsson T, Westling G, Johansson RS, Forssberg H. Cortical activity in precision- versus power-grip tasks: an fMRI study. *J Neurophysiol* 2000; 83: 528–36.
- Ehrsson HH, Fagergren E, Forssberg H. Differential fronto-parietal activation depending on force used in a precision grip task: an fMRI study. *J Neurophysiol* 2001; 85: 2613–23.
- Eliasson AC, Gordon AM, Forssberg H. Basic co-ordination of manipulative forces of children with cerebral palsy. *Dev Med Child Neurol* 1991; 33: 661–70.
- Eliasson AC, Gordon AM, Forssberg H. Impaired anticipatory control of isometric forces during grasping by children with cerebral palsy. *Dev Med Child Neurol* 1992; 34: 216–25.
- Eliasson AC, Gordon AM, Forssberg H. Tactile control of isometric fingertip forces during grasping in children with cerebral palsy. *Dev Med Child Neurol* 1995; 37: 72–84.
- Flanagan JR, Wing AM. The role of internal models in motion planning and control: evidence from grip force adjustments during movements of hand-held loads. *J Neurosci* 1997; 17: 1519–28.
- Forssberg H. Neural control of human motor development. [Review]. *Curr Opin Neurobiol* 1999; 9: 676–82.
- Forssberg H, Eliasson AC, Kinoshita H, Johansson RS, Westling G. Development of human precision grip. I: basic coordination of force. *Exp Brain Res* 1991; 85: 451–7.
- Forssberg H, Kinoshita H, Eliasson AC, Johansson RS, Westling G, Gordon AM. Development of human precision grip. II. Anticipatory control of isometric forces targeted for object's weight. *Exp Brain Res* 1992; 90: 393–8.
- Forssberg H, Eliasson AC, Redon-Zouitenn C, Mercuri E, Dubowitz L. Impaired grip-lift synergy in children with unilateral brain lesions. *Brain* 1999; 122: 1157–68.
- Forssberg H, Ingvarsson PE, Iwasaki N, Johansson RS, Gordon AM. Action tremor during object manipulation in Parkinson's disease. *Mov Disord* 2000; 15: 244–54.
- Fukui K, Iguchi I, Kito A, Watanabe Y, Sugita K. Extent of pontine pyramidal tract Wallerian degeneration and outcome after supratentorial hemorrhagic stroke. *Stroke* 1994; 25: 1207–10.
- Galea MP, Darian-Smith I. Multiple corticospinal neuron populations in the macaque monkey are specified by their unique cortical origins, spinal terminations, and connections. *Cereb Cortex* 1994; 4: 166–94.
- Galea MP, Darian-Smith I. Corticospinal projection patterns following unilateral section of the cervical spinal cord in the newborn and juvenile macaque monkey. *J Comp Neurol* 1997a; 381: 282–306.
- Galea MP, Darian-Smith I. Manual dexterity and corticospinal connectivity following unilateral section of the cervical spinal cord in the macaque monkey. *J Comp Neurol* 1997b; 381: 307–19.
- Gibbs J, Harrison LM, Stephens JA, Evans AL. Does abnormal branching of inputs to motor neurones explain abnormal muscle cocontraction in cerebral palsy? *Dev Med Child Neurol* 1999; 41: 465–72.
- Gordon AM. Development of anticipatory control mechanisms for manipulation. In: Forssberg H, Hirschfeld H, editors. *Movement disorders in children*. Medicine and sport science, Vol. 36. Basel: Karger; 1992. p. 130–6.
- Gordon AM, Duff SV. Fingertip forces during object manipulation in children with hemiplegic cerebral palsy. I: anticipatory scaling. *Dev Med Child Neurol* 1999a; 41: 166–75.
- Gordon AM, Duff SV. Relation between clinical measures and fine manipulative control in children with hemiplegic cerebral palsy. *Dev Med Child Neurol* 1999b; 41: 586–91.
- Gordon AM, Forssberg H, Johansson RS, Eliasson AC, Westling G. Development of human precision grip. III. Integration of visual size cues during the programming of isometric forces. *Exp Brain Res* 1992; 90: 399–403.
- Gordon AM, Westling G, Cole KJ, Johansson RS. Memory representations underlying motor commands used during

- manipulation of common and novel objects. *J Neurophysiol* 1993; 69: 1789–96.
- Gordon AM, Charles J, Duff SV. Fingertip forces during object manipulation in children with hemiplegic cerebral palsy. II: bilateral coordination. *Dev Med Child Neurol* 1999; 41: 176–85.
- He SQ, Dum RP, Strick PL. Topographic organization of corticospinal projections from the frontal lobe: motor areas on the lateral surface of the hemisphere. *J Neurosci* 1993; 13: 952–80.
- He SQ, Dum RP, Strick PL. Topographic organization of corticospinal projections from the frontal lobe: motor areas on the medial surface of the hemisphere. *J Neurosci* 1995; 15: 3284–306.
- Jeannerod M, Arbib MA, Rizzolatti G, Sakata H. Grasping objects: the cortical mechanisms of visuomotor transformation. [Review]. *Trends Neurosci* 1995; 18: 314–20.
- Johansson RS, Westling G. Coordinated isometric muscle commands adequately and erroneously programmed for the weight during lifting task with precision grip. *Exp Brain Res* 1988; 71: 59–71.
- Johnson LM, Randall MJ, Reddiough DS, Oke LE, Byrt TA, Bach TM. Development of a clinical assessment of quality of movement for unilateral upper-limb function. *Dev Med Child Neurol* 1994; 36: 965–73.
- Jones RD, Donaldson IM, Parkin PJ. Impairment and recovery of ipsilateral sensory-motor function following unilateral cerebral infarction. *Brain* 1989; 112: 113–32.
- Kuhtz-Buschbeck JP, Ehrsson HH, Forssberg H. Human brain activity in the control of fine static precision grip forces: an fMRI study. *Eur J Neurosci* 2001; 14: 382–90.
- Lemon RN. Neural control of dexterity: what has been achieved? [Review]. *Exp Brain Res* 1999; 128: 6–12.
- Marin-Padilla M. Developmental neuropathology and impact of perinatal brain damage. II: white matter lesions of the neocortex. [Review]. *J Neuropathol Exp Neurol* 1997; 56: 219–35.
- Marque P, Felez A, Puel M, Demonet JF, Guiraud-Chaumeil B, Roques CF, et al. Impairment and recovery of left motor function in patients with right hemiplegia. *J Neurol Neurosurg Psychiatry* 1997; 62: 77–81.
- Mathiowetz V, Rogers SL, Dowe-Keval M, Donahoe L, Rennells C. The Purdue Pegboard: norms for 14- to 19-year-olds. *Am J Occup Ther* 1986a; 40: 174–9.
- Mathiowetz V, Wiemer DM, Federman SM. Grip and pinch strength: norms for 6- to 19-year-olds. *Am J Occup Ther* 1986b; 40: 705–11.
- Mercuri E, Jongmans M, Bouza H, Haataja L, Rutherford M, Henderson S, et al. Congenital hemiplegia in children at school age: assessment of hand function in the non-hemiplegic hand and correlation with MRI. *Neuropediatrics* 1999; 30: 8–13.
- Miyai I, Suzuki T, Kii K, Kang J, Kubota K. Wallerian degeneration of the pyramidal tract does not affect stroke rehabilitation outcome. *Neurology* 1998; 51: 1613–6.
- Nakajima K, Maier MA, Kirkwood PA, Lemon RN. Striking differences in transmission of corticospinal excitation to upper limb motoneurons in two primate species. *J Neurophysiol* 2000; 84: 698–709.
- Niemann G, Grodd W, Schoning M. Late remission of congenital hemiparesis: the value of MRI. *Neuropediatrics* 1996; 27: 197–201.
- Olivier E, Edgley SA, Armand J, Lemon RN. An electrophysiological study of the postnatal development of the corticospinal system in the macaque monkey. *J Neurosci* 1997; 17: 267–76.
- Passingham RE, Perry VH, Wilkinson F. The long-term effects of removal of sensorimotor cortex in infant and adult rhesus monkeys. *Brain* 1983; 106: 675–705.
- Paus T, Zijdenbos A, Worsley K, Collins DL, Blumenthal J, Giedd JN, et al. Structural maturation of neural pathways in children and adolescents: in vivo study. *Science* 1999; 283: 1908–11.
- Pennock JM, Rutherford MA, Cowan FM, Bydder GM. MRI: early onset of changes in Wallerian degeneration. *Clin Radiol* 1993; 47: 311–4.
- Pereira HS, Landgren M, Gillberg C, Forssberg H. Parametric control of fingertip forces during precision grip lifts in children with DCD (developmental coordination disorder) and DAMP (deficits in attention motor control and perception). *Neuropsychologia* 2001; 39: 478–88.
- Porter R, Lemon R. Corticospinal function and voluntary movement. Oxford: Clarendon Press; 1993.
- Randall M, Johnson L, Reddiough D. The Melbourne assessment of unilateral upper limb function, test administration manual. Melbourne: Royal Children's Hospital; 1999.
- Rouiller EM, Yu XH, Moret V, Tempini A, Wiesendanger M, Liang F. Dexterity in adult monkeys following early lesion of the motor cortical hand area: the role of cortex adjacent to the lesion. *Eur J Neurosci* 1998; 10: 729–40.
- Sawlani V, Gupta RK, Singh MK, Kohli A. MRI demonstration of Wallerian degeneration in various intracranial lesions and its clinical implications. *J Neurol Sci* 1997; 146: 103–8.
- Staudt M, Niemann G, Grodd W, Krageloh-Mann I. The pyramidal tract in congenital hemiparesis: relationship between morphology and function in periventricular lesions. *Neuropediatrics* 2000; 31: 257–64.
- Steenbergen B, Hulstijn W, Lemmens IH, Meulenbroek RG. The timing of prehensile movements in subjects with cerebral palsy. *Dev Med Child Neurol* 1998; 40: 108–14.
- Talairach J, Tournoux P. Co-planar stereotaxic atlas of the human brain: 3-dimensional proportional system: an approach to cerebral imaging. Stuttgart: Thieme; 1988.
- Thilmann AF, Fellows SJ, Garms E. Pathological stretch reflexes on the "good" side of hemiparetic patients. *J Neurol Neurosurg Psychiatry* 1990; 53: 208–14.
- Vandermeeren Y, Olivier E, Sébire G, Cosnard G, Bol A, Sibomana M, et al. Increased FDG uptake in the ipsilesional sensorimotor cortex in congenital hemiplegia. *Neuroimage* 2002a; 15: 949–60.
- Vandermeeren Y, De Volder A, Bastings E, Thonnard J-L, Duqué J,

Grandin C, et al. Functional relevance of abnormal fMRI activation pattern after unilateral schizencephaly. *Neuroreport* 2002b; 13: 1821–4.

Westling G, Johansson RS. Factors influencing the force control during precision grip. *Exp Brain Res* 1984; 53: 277–84.

Witney AG, Vetter P, Wolpert DM. The influence of previous experience on predictive motor control. *Neuroreport* 2001a; 12: 649–53.

Witney AG, Wing AM, Thonnard JM, Smith AM. Feedforward and feedback contributions to precision grip. In: Gantchev N, editor.

From basic motor control to functional recovery—II. Varna: MCC; 2001b. p. 163–76

Wolpert DM, Flanagan JR. Motor prediction. [Review]. *Curr Biol* 2001; 11: R729–32.

Wolpert DM, Ghahramani Z, Flanagan JR. Perspectives and problems in motor learning. *Trends Cogn Sci* 2001; 5: 487–94.

Received March 6, 2002. Revised July 30, 2002.

Accepted September 8, 2002.