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Temporary and permanent signs of interhemispheric disconnection after traumatic brain injury

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Abstract

The corpus callosum is frequently damaged by closed head traumas, and the resulting deficits of interhemispheric communication may vary according to the specific position of the lesion within the corpus callosum. This paper describes a single case who suffered a severe traumatic brain injury resulting in a lesion of the posterior body of the corpus callosum. Among the classical symptoms of interhemispheric disconnection, left hand anomia, left upper limb ideomotor dyspraxia, left visual field dyslexia and dysnomia, and left ear suppression in a dichotic listening task were observed shortly after the injury but recovered completely or almost completely with the passage of time. The only symptom of interhemispheric disconnection which was found to persist more than 4 years after the injury was an abnormal prolongation of the crossed-uncrossed difference in a simple visuomotor reaction time task. This prolongation was comparable with that observed in subjects with complete callosal lesions or agenesis. The results suggest that the posterior body of the corpus callosum may be an obligatory interhemispheric communication channel for mediating fast visuo-motor responses. The transient nature of other symptoms of interhemispheric disconnection suggests a relatively wide dispersion of fibers with different functions through the callosal body, such that parts of them can survive a restricted lesion and allow functional recovery of hemispheric interactions. An assessment of the evolution in time of symptoms of interhemispheric disconnection following restricted callosal lesions may reveal fine and coarse features of the anatomo-functional topography of the corpus callosum.

Keywords: CUD; Corpus callosum; Head trauma

1. Introduction

Closed head trauma (CHT) can not only damage the gray matter of the brain, but also cause direct injury to the cerebral white matter by vascular disruption and edema, as well as by shear and stretch forces that distort and interrupt nerve axons. The corpus callosum is particularly vulnerable to such injuries, as shown by neuropathological [8,38], neurochemical [9,35], and neuroimaging investigations [15,54,56]. After a CHT one can therefore expect the appearance of symptoms of interhemispheric disconnection (ID), similar to those that are observed as a result of surgical callosal sections [23,50], or spontaneous, non-traumatic callosal lesions associated with vascular, tumoral or degenerative brain diseases (reviews in [7,10]).

Reports of ID symptoms caused by traumatic callosal damage are nevertheless relatively few, and in many cases the anatomofunctional interpretation of the symptomatology is complicated by the co-occurrence of direct callosal damage and unilateral or bilateral hemispheric lesions. Typical ID symptoms found in single cases after CHT include left ideomotor apraxia [11,21,47,48,58], right or bilateral constructional apraxia [11,57,58], left agraphia [14,47,57,58], left tactile anomia [13,21,36,37,57,58], impaired intermanual transfer of somesthetic information [14,21,36,37,57,58], left alien hand and diagonistic dyspraxia [13,24], impaired bimanual coordination [36,57], impaired left ear performance in dichotic verbal tasks [2,14,37,57], left hemialexia and left visual anomia [14,57,58]. Traumatic callosal lesions are usually partial, and the occurrence of one or the other of these symptoms may depend on the site of the lesion within the corpus callosum. Obvious ID symptoms however are thought to appear only after considerably large traumatic callosal lesions [47,57], and a strict systematic

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correlation between a specific ID symptom and a lesion of a specific portion of the corpus callosum is still lacking. In addition, ID symptoms from partial callosal lesions may be reversible in time, possibly because of the waning of temporary callosal damage, such as that dependent on edema, or due to functional compensation by intact contingents of callosal fibers.

In the present paper, we report a longitudinal study of ID symptoms in a single case with a traumatic lesion restricted to the posterior body of the corpus callosum, with particular reference to a so-far largely neglected potential effect of callosal damage, namely, the increase of the crossed-uncrossed difference (CUD) in simple visuomotor reaction time (RT). In a task requiring subjects to press a key with the right or left hand in response to a light stimulus in the right or left visual field, uncrossed responses, made with the hand ipsilateral to the stimulated field, are faster than crossed responses, made with the hand contralateral to the stimulated field, by about 2–3 ms. Since each hemisphere receives inputs from the contralateral visual field and controls movements of the contralateral hand, it is argued that the neural pathway for uncrossed responses, being contained within one hemisphere, is shorter than the neural pathway for crossed responses, which should include a passage from the hemisphere receiving the light stimulus to the hemisphere controlling the responding hand. The normal CUD of 2–3 ms can therefore be regarded as a measure of interhemispheric transfer time, and more specifically of callosal transfer time [3,6,19,29,39]. It has indeed been found that in subjects with callosal sections or agenesis, the CUD is at least an order of magnitude greater than the normal CUD, suggesting that in the absence of the corpus callosum a time-consuming interhemispheric transfer is effected by non-callosal cross-midline pathways [1,18,41]. We found a permanent CUD prolongation associated with a partial callosal lesion from CHT, contrasting with other ID symptoms that were clearly apparent shortly after the trauma, but disappeared later on in the course of recovery.

2. Methods

OG, a 20 years-old workman with 10 years of schooling and no history of major illnesses, suffered a severe CHT in a car accident on 7 September 1996. On hospital admission he was comatose with a post-intubation Glasgow Coma score of 7 (E1, V1, M5). A first CT scan revealed blood deposition in the ventricular spaces and several multiple subcortical contusions. His stay in intensive care was marked by a slow but steady recovery of neurological functions. At 5 weeks post-injury he was removed from mechanical respiration, and 2 weeks later he was able to follow simple verbal commands. Further CT scans documented a re-absorption of blood in the ventricular spaces and an improvement in the subcortical contusions. At the end of October he had completely regained consciousness and therefore was transferred to a rehabilitation unit, where he remained for about 4 months. At the time of discharge from the unit, a slight hypostenia and ataxia of the left upper limb, as sequelae of a slight left-sided hemiparesis, were still detectable, in the absence of any other apparent neurological deficit. In an MRI examination carried out a few days before discharge, approximately 5 months post-injury, T1- and T2-weighted images showed bilateral, extra-cerebral, frontal areas of high signal intensity which have been interpreted as subdural hygromas with high proteinaceus content. Moreover, several focal areas of low signal intensity (not detectable on CT scans) in both T1- and T2-weighted images were present bilaterally in the frontal lobes, in the left temporo-polar region, close to the frontal horn of the left lateral ventricle, in the right thalamus, in the right paratrigonal region, and in the posterior third of the body of the corpus callosum (Fig. 1a). All these areas of low signal intensity could be regarded as sequelae of multiple deep contusions.

After discharge from the rehabilitation unit, motor and cognitive retraining was continued, finally allowing the patient to resume his job in May 1998. Three years later, when the patient was leading a fully normal life, a follow-up MRI showed persistence of previously described hemosiderin deposits in sites of deep contusions, along with a marked atrophy of the posterior third of the body of the corpus callosum with a minimal involvement of the splenium, which appeared substantially preserved on the midline (Fig. 1b), although in coronal and transversal sections a moderate degree of atrophy appeared to affect some contingents of splenial fibers on the right side. The bilateral subdural hygromas had disappeared.

A reliable neuropsychological evaluation was possible only 4 months after the injury when patient OG was fully alert, well oriented as to time and space, and did not show any instability of mood or behavioral disturbances. The presence of a slight left-sided visual and tactile neglect and extinction was suggested by the results of the Albert Cancellation Test and tests of reading and drawing from copy, and by a tendency to miss left visual and tactile stimuli on bilateral stimulation. All these deficits had disappeared when the patient was retested approximately 7 months after injury. At that time, however, the results of the Verbal Fluency and Trail-Making tests, as well as of the Wisconsin Card Sorting Test, suggested a modest impairment of executive functions. The patient's overall level of intellective functioning was in the below-average range (full-scale IQ = 85) with a significant advantage of verbal (VIQ = 100) over performance IQ (PIQ = 72). A moderate impairment of intellective functioning was also confirmed by his performance on the Raven Progressive Matrices (score = 24/48). These deficits were not permanent, since in January 2000, more than 3 years after the injury, the patient's performance was well within the normal range on the Verbal Fluency and Trail-Making tests, and good on the Raven Progressive Matrices (score = 34/48). Finally, when assessed for hand preference by means of Briggs

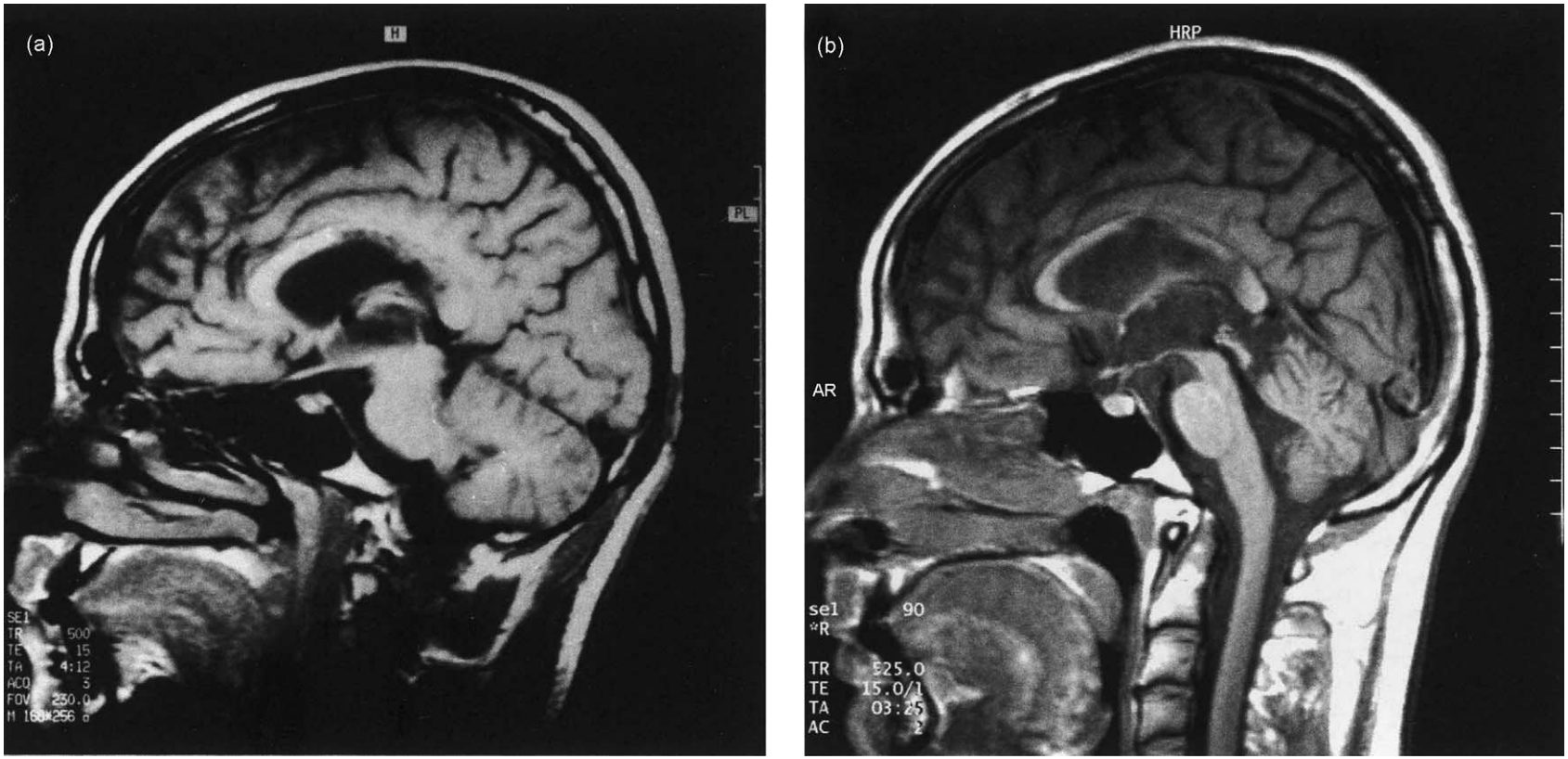

Fig. 1. MR T1-weighted sagittal scans showing OG's callosal lesions 5 months post-injury (a) and 3.5 years later (b). Damaged fibers appear as areas of low signal intensity within the corpus callosum. The exams were performed on (a) February 15th, 1997, and (b) February 17th, 2000, respectively. See text for details.

and Nebes's questionnaire [12], OG qualified as a full right-handed subject.

An extensive assessment of callosal functions was carried out in several separate sessions throughout the post-acute period between January and May 1997, whereas follow-up evaluations were carried out between January 2000 and February 2001.

The *haptic recognition test* involved the palpation of one of a series of several common objects at a time with the right or left hand out of view. The sample included 28 common objects of everyday use. In addition, plastic letters and digits were used as verbal stimuli whose recognition presumably engages the left hemisphere more than the right. The subject had simply to name the object, without limitations on time for responding. In a further test, two objects were placed one in each hand of the subject, and he was to tell whether they were the same or different. "Same" responses were to be given to physically identical objects, and "different" responses were to be given to physically different objects, even if semantically related (e.g. two keys of different make and size).

In the *tactile localization test* the blindfolded subject was seated with the forearms resting on a table with the palms of the hands facing up. On each trial the examiner touched the centerpoints of the distal phalange of one of the four fingers and immediately thereafter the subject was to touch the stimulated point with the thumb of the same hand (intramanual condition), or the corresponding point of the homonymous finger of the other hand with the thumb of that hand (intermanual condition). Each testing session included 20 stimuli delivered in random succession to the 4 positions in both the intramanual and the intermanual conditions. Each hand was tested in the intramanual condition and each direction of transfer was tested in the intermanual condition.

The *test for praxis* involved the execution of various common symbolic gestures with either hand upon an appropriate verbal command. In case of a failed or inappropriate response to a verbal command, the examiner made the required gesture and the subject was asked to imitate it.

In the *tachistoscopic reading test*, the subject sat in front of a computer monitor at a distance of 57 cm. from it. Stimuli consisted of 40 four-letter high-frequency Italian nouns presented in a horizontal or vertical orientation to the right or left of a fixation point. Stimulus duration was 150 ms. Each noun subtended a solid visual angle of 6.2° by 1°, and the distance between the fixation point and the nearest part of the noun was 2.3°. In an experimental session each of the 40 nouns was presented two times, one in the right field and the other in the left field; the sequence of the nouns and the alternation between right-field and left-field stimuli were random. Each noun presentation was preceded by an acoustic warning stimulus which prompted the subject to look at the fixation mark and to maintain fixation until after the presentation of the noun, 500–1000 ms after the sound. Fixation maintenance was monitored by means of a videocamera. The subject was to read aloud the noun presented on each trial; no forced responses were required and there was no time limitation for responding. Each trial was terminated after recording the subject's response and the next trial was started by the experimenter.

The *tachistoscopic object recognition test* was similar in design and procedure to the tachistoscopic reading test, except that the patient was requested to name 80 drawings of items belonging to different semantic categories (animals, fruits, musical instruments, vehicles, clothing, domestic electrical appliances, common objects), tachistoscopically presented in the left or right visual fields for 150 ms. In addition, 144 trials were run in which two object pictures or drawings were tachistoscopically and simultaneously presented one in the left field and the other in the right field. The patient was requested to judge the items as same or different, and then to name them. There were 72 "same" pairs and 36 "different" pairs; each of the latter pairs was presented twice, so that each member of a pair appeared once in the right field and once in the left field.

In the *dichotic listening test*, a trial consisted in the simultaneous presentation through headphones of tape-recorded series of four digits, spoken by a male voice. One series was presented to the right ear and the other was presented to the left ear. Immediately after the presentation the patient was to report, in a free order, all the digits he remembered to have heard. Each testing session was made up of 40 trials, and the pairing of the digits in the two series of a trial was such that digits occurring simultaneously were always different. Monaural performance was checked by presenting single series to each ear separately.

In the *CUD assessment test*, the subject was seated in a dimly lit room with his head positioned in a forehead and chin rest at a 57 cm distance from a 20-in Nec/Multisync 5D monitor screen controlled by an IBM-compatible computer by means of a commercial software (MEL2, Psychology Software Tools Inc.). Visual stimuli were white square 1 cm for side, and 9.2 cd/cm^2 luminance, flashed for 33.2 ms, according to a completely random sequence, to the right or left of a white cross which served as a fixation mark. The subject's task was to fixate on the central cross and respond as quickly as possible to the visual stimulus by pressing with the index finger a key mounted on a key-box. Maintenance of fixation was monitored by a videocamera and trials with failure to fixate were aborted by the examiner. An acoustic tone was used as a warning signal. The intervals between acoustic signal and stimulus presentation varied unpredictably between 200 and 700 ms. The intertrial interval was in the range of 1.000–1.800 ms. In each testing day two sessions were run: one with the stimulus at 4°, and one with the stimulus at 8°. Each session involved four blocks, each of which consisted of 50 trials; the responding hand varied throughout the blocks according to a Latin square design (right–left–left–right), counterbalanced across the sessions. Thus, for each eccentricity, the subject performed 200 trials, 50 for each of four hand/visual field combinations. Mean RTs for each hand/visual field were used to

estimate the CUD in each session. Five right-handed, male subjects matched in age, served as controls.

3. Results

3.1. Haptic denomination with the left hand

When tested 4 months after injury, OG showed a severe left hand haptic anomia, i.e. a hallmark of interhemispheric disconnection attributable to the interruption of a callosal somesthetic input to the language-dominant left hemisphere [10]. He failed to name 21 items out of 28 held in the left hand, whereas performance with the right hand was errorless. Subsequently, however, performance with the left hand showed a strong improvement, so that 1 month later he recognized 10 objects out of 12, while in two subsequent tests run 1 and 2 months later he made no naming errors (20 correct out of 20, in both cases). Forty months after injury, accuracy with either hand was again perfect, even when stimuli consisted of "verbal" items such as plastic letters and digits. Moreover, at that time OG performed at ceiling when he was required to judge as same or different two objects separately presented to the two hands. An initially defective interhemispheric transfer of haptic information, best accounted for by a callosal dysfunction, was thus followed by a complete functional restitution, most probably mediated by callosal fibers that had not been affected by the lesion or had recovered their function.

3.2. Localization of tactile stimulation and transfer of somesthetic information

At no time during the test period did OG show any difficulty in localizing stimuli on both right and left fingers, as well as in transferring exact spatial information from the right hand to the left, and vice versa. This good performance is in keeping with recent results indicating that the location of callosal lesions responsible for somesthetic ID symptoms is anterior to that of the OG's callosal lesion [30].

3.3. Praxis

A modest but clear-cut impairment of left upper limb gestures on verbal command, as well as on imitation, was noted during several months after the trauma. In the testing situation, all of the patient's left upper limb gestures made it clear that he could ideate the required movement, but not execute it correctly, suggesting the presence of a left ideomotor apraxia. In contrast, head, ocular, and facial movements, as well as right upper limb gestures, were always executed in an accurate manner. The left ideomotor apraxia progressively recovered, and 40 months after injury all types of left upper limb gestures to verbal command or imitation appeared normal. During the entire observation period, OG never complained of any "alien hand" sign, nor did he exhibit any evidence of diagonistic dyspraxia, i.e. of obvious conflict between the two hands in bimanual movements. Moreover, copying and block design tasks did not disclose any sign of constructional apraxia for either hand.

3.4. Tachistoscopic reading

As indicated in Table 1, OG's performance fell short of complete accuracy in either visual field with both horizontal and vertical presentations, but the number of errors was consistently greater in the left visual field than in the right (mean performance across sessions: left visual field 20 correct out of 40; right visual field 31.6 correct out of 40, $\chi^2(1) = 6.06$, $P < 0.05$).

In the first three sessions the noun stimuli were presented in a horizontal arrangement. In the first two sessions, performance in the left field was significantly inferior to that in the right field, but in the third session the difference between the two hemifields did not reach statistical significance (Table 1). However, in the fourth session, a significant difference in the same direction re-emerged with a vertical noun presentation, which increased the difficulty of the task. In a further test run 54 months after injury, vertical noun presentation yielded a relatively good performance in both hemifields, and the interfield difference in favor of the right field was not significant (see Table 1).

3.5. Tachistoscopic object recognition

Tests run 46 months after the trauma revealed a mild left field hemianomia: OG failed to name two items out of forty presented in the right visual field, and 10 items out of 40 presented in the left visual field ($\chi^2(1) = 4.74$, $P < 0.05$). In a same/different matching task run at the same time, OG responded correctly on all the "same" trials, but judged as "same" eleven out of 72 "different" trials. In 7 out of the 11 errors, the items were semantically and perceptually related (e.g. cat and dog). When requested to report the items he saw on trials in which he produced a wrong "same" response, he consistently reported the item presented in the RVF. When retested 7 months later, he showed a marked improvement, so that in the naming test there was no statistically significant difference between the two fields (two errors in the right field, and five errors in the left field: $\chi^2(1) = 0.62$, n.s.), and in the same/different matching task he made errors only on two different trials.

3.6. Dichotic listening task

Four months after the trauma, the patient was extremely accurate in reporting series of four digits presented monoaurally to either ear. However, when tested in a dichotic listening paradigm, he showed an almost complete left-ear suppression, being able to report only one digit out of 40 presented to the left ear, as against a report of 39 digits out of 40 presented to the right ear ($\chi^2(1) = 67.59$, $P < 0.001$).

Table 1
Tachistoscopic reading: numbers of correct responses to lateralized noun stimuli in different post-trauma sessions

	Session											
	I			II			III			IV			Follow-up		
Months from injury	5			6			7			7			54		
	LVF	RVF		LVF	RVF		LVF	RVF		LVF	RVF		LVF	RVF	
Noun presentation	Horizontal	Horizontal		Horizontal	Horizontal		Horizontal	Horizontal		Vertical	Vertical		Vertical	Vertical	
Score/40	13	27		16	31		26	32		14	31		31	37	
	$X^2 = 8.34$, d.f.1 $P < 0.01$			$X^2 = 9.98$, d.f.1 $P < 0.01$			$X^2 = 1.55$, d.f.1 n.s.			$X^2 = 2.84$, d.f.1 $P < 0.001$			$X^2 = 2.42$, d.f.1 n.s.		

The left ear score hardly improved when he was explicitely required to ignore digits presented to the right ear and report only digits presented to the left ear (left ear score = 2/40, right ear score = 38/40; $\chi^2(1) = 60.48$, $P < 0.001$). This striking left ear suppression was no longer present on a subsequent test carried out 3 months later, in which OG reported 25 out of 40 digits presented to the left ear, and 29 out of 40 digits presented to the right ear ($\chi^2(1) = 0.51$, n.s.).

3.7. Interhemispheric transmission time

RTs shorter than 150 ms and longer than 600 ms were considered as anticipations and retardations, respectively, and were not included in the analyses. As a result, 36 acceptable RTs were available for each hand-field combination for each eccentricity for each session, and were entered into a repeated measures ANOVA with stimulus eccentricity, session, field and hand as main factors. The mean results, along with the significant sources of variation in the ANOVA, are presented in Table 2.

The statistically significant effects can be summarized as follows. RT was faster with stimuli at the 4° eccentricity than with stimuli at the 8° eccentricity, in accordance with the different photopic sensitivity of the retina at the two eccentricities [16]. RT increased from the first session to the third session, and the RT increase was greater for the left hand than for the right hand. There was a significant disadvantage for the left field compared to the right field, and for the left hand compared to the right hand. The disadvantage of the left hand relative to the right hand was greater with stimuli in the right field than with stimuli in the left field; it was also greater with stimuli at the 8° eccentricity than with stimuli at the 4° eccentricity. In addition, the differences between the hands in each field were greater at the 8° eccentricity than at the 4° eccentricity. Taken together with the early transient signs of left neglect and extinction and left limb motor disturbances, the RT differences between the hands and between the visual fields can be regarded as sensitive indexes of a minor but lasting dysfunction of the right hemisphere. The long lasting nature of this dysfunction is supported by the insignificance of the field/session interaction ($F(2, 70) = 1.70$, n.s.), as well as by the increase of the disadvantage of the left hand across sessions, as indicated by the significant session/hand interaction (Table 2).

The logic of the CUD assessment is that all systematic differences in favor of one field and/or one hand cancel out if one compares the mean RTs of ipsilateral and contralateral responses of both hands. Overall ipsilateral RT, i.e. the mean between RTs of the right hand to right field stimuli and RTs of the left hand to left field stimuli, was 303.7 ms, while overall contralateral RT, i.e. the mean of RTs of the right hand to left field stimuli and RTs of the left hand to right field stimuli, was 326.4. The mean contralateral–ipsilateral difference, significant at a $P < 0.001$ level ($F(1, 35) = 23.58$), corresponds to a net CUD of 22.7 ms, a value that falls definitely above the upper limit of the range of the five normal

Table 2
Reaction time (mean values in ms ± S.D.) as a function of different factors and their interactions in the ANOVA

Stimulus eccentricity, $F(1, 35) = 13.60$, $P = 0.001$		
4° = 306.6 ± 83.6	8° = 323.5 ± 74.9	
Session, $F(2, 70) = 146.56$, $P < 0.001$		
First = 272.9 ± 63.0	Second = 301.5 ± 75.2	Third = 370.7 ± 86.0
Field, $F(1, 35) = 32.71$, $P < 0.001$		
Left = 329.7 ± 82.1	Right = 300.4 ± 86.8	
Hand, $F(1, 35) = 59.19$, $P < 0.001$		
Left = 335.7 ± 83.8	Right = 294.4 ± 82.7	
Stimulus eccentricity/hand interaction, $F(1, 35) = 30.19$, $P < 0.001$		
4°, left = 315.5 ± 80.3	8°, left = 355.9 ± 82.5	
4°, right = 297.7 ± 86.0	8°, right = 291.1 ± 79.3	
Session/hand interaction, $F(2, 70) = 8.99$, $P < 0.001$		
First, left = 287.7 ± 66.5	Second, left = 314.3 ± 60.6	Third, left = 405.1 ± 73.8
First, right = 258.2 ± 55.8	Second, right = 288.7 ± 85.8	Third, right = 336.3 ± 83.8
Field/hand interaction, $F(1, 35) = 23.58$, $P < 0.001$		
Left field, left hand = 339.0 ± 85.0	Right field, left hand = 332.4 ± 82.7	
Left field, right hand = 320.4 ± 78.2	Right field, right hand = 268.4 ± 78.9	
Stimulus eccentricity/field/hand interaction, $F(1, 35) = 6.07$, $P < 0.02$		
4°, left field, left hand = 324.0 ± 83.8	8°, left field, left hand = 353.9 ± 83.9	
4°, left field, right hand = 319.0 ± 83.5	8°, left field, right hand = 321.9 ± 73.0	
4°, right field, left hand = 307.0 ± 76.2	8°, right field, left hand = 357.8 ± 81.4	
4°, right field, right hand = 276.4 ± 83.4	8°, right field, right hand = 260.4 ± 77.6	

Only the significant sources of variation are mentioned.

controls tested in the same experimental setting (mean CUD = 2.8, range = −0.67–5.56), and is nearly an order of magnitude greater than the mean CUDs reported for normal observers in several studies (reviews in [3,39]). On the other hand, OG's prolonged CUD is comparable with those reported for subjects with complete callosal agenesis [41], and it falls within the range reported for callosotomy cases [1,6,18,28]. The overall CUD was 52 ms for the right hand and −6.6 ms for the left hand, the negative CUD for the left hand depending on the net 29.3 ms left field disadvantage. The CUD for the 8° stimulus eccentricity (32.6 ms) was more than twice as long as the CUD for the 4° stimulus eccentricity (12.8 ms), as reflected by the significant three-way interaction between stimulus eccentricity, hand and field in the ANOVA (Table 2). Unlike the general increase in RT from the first to the third session, the CUD value did not change significantly across sessions (first session 27.1 ms; second session 13.4 ms; third session 27.5 ms), as indicated by the insignificant F value of the session/hand/field interaction in the ANOVA ($F(2, 70) = 1.33$, n.s.).

4. Discussion

The transient deficits in executive and intellective functions shown by OG shortly after the head trauma were most probably due to the extracallosal brain damage. The temporary motor deficits of the left limbs, and the slight and short lasting left sided visual and tactile neglect can be attributed to a similar extracallosal cause, that is to a right hemisphere dysfunction. A contribution from a callosal disconnection to these symptoms cannot completely be excluded, in view of left neglect-like symptoms occasionally occurring in callosotomy patients [5]. Although the more marked symptoms attributable to a right hemisphere damage were no longer apparent at 7 months after injury, the persistent disadvantages of the left visual field and the left hand for simple RT attest the stable existence of a minor right hemisphere dysfunction.

The present patient's symptoms that are clearly suggestive of an ID are a pathological increase in the CUD, an ideomotor apraxia of the left upper limb, a modest alexia in the left visual field, and a left ear suppression in verbal dichotic tests. Only the CUD increase was still detectable at the latest post-injury tests, and its persistence at 4 years after the trauma suggests that it may be a permanent ID symptom. A number of years ago Rubens et al. [47] and Geschwind [25] argued that ID symptoms due to spontaneous callosal lesions are frequently overlooked in neurological practice because routine methods of examination do not include specific tests for bearing out such symptoms. As a result, most of our knowledge about ID symptoms has come from the relatively few cases that were submitted to surgical callosal lesions for the control of drug-resistant forms of epilepsy [23,50]. Recently, however, studies of patients with closed head trauma or other spontaneous pathologies of the central nervous system have reported a number of ID effects attributable to callosal lesions (e.g. [4,31,34,36]). With one single exception [24], common to such investigations has been the failure to test for a pathological increase in interhemispheric transfer

time in simple visuomotor reaction time tasks, as indexed by the abnormally elevated CUD values which are consistently found in patients with surgical or non-traumatic callosal lesions or in subjects with corpus callosum agenesis (e.g. [1,18,41]). In principle, it is possible that CUD measures are a more sensitive index of partial interhemispheric disconnection compared to clinical signs or other forms of tachistoscopic assessment. In the only study that assessed the CUD in a case with a vascular callosal lesion comparable for location and extent to the present one, the CUD was abnormally prolonged with stimuli in the right field, and insignificantly negative in the left field [24]. Like OG, the patient of that study showed a slowed reactivity of the left field and the left hand, but the most conspicuous symptom was an "alien" behavior of the left hand which was totally absent in OG.

The present study provides the first evidence for a long-standing above-normal CUD values in a patient with a post-traumatic partial lesion of the corpus callosum. As in the patient of Geschwind et al. [24], OG's prolonged CUD was apparent only with right field stimuli, since with left field stimuli there was a slightly negative CUD. In OG and the patient of Geschwind et al. [24] alike, this asymmetry is best attributed to a slight post-lesional right hemisphere dysfunction, and does not conflict with the conclusion of a general increase of interhemispheric transfer time in simple visuomotor reactions. A systematic difference that favors one field and/or one hand is indeed eliminated by averaging ipsilateral and contralateral RTs, and any abnormal prolongation of the CUD that remains after averaging is bound to reflect a real defect of interhemispheric transfer. Thus, to the extent that reasonable conclusions can be drawn from a single case, this finding points to immediately pre-splenial portions of the corpus callosum as containing the fibers that mediate fast interhemispheric transfer for making simple responses with one hand to contralateral visual stimuli. This indication is in keeping with previous inferences that in the intact brain the interhemispheric transfer for fast visuomotor responses occurs beyond the initial stage of visual information processing, probably at a premotor level involving parietal callosal connections coursing anteriorly to the splenium [53]. The CUD is indeed known to be normal or near normal after extensive anterior callosotomies which spare the posterior third of the corpus callosum, whereas an intact splenium, containing all the callosal connections of the visual cortices, does not appear sufficient by itself for ensuring a normal CUD [55]. In the absence of the callosal fibers mediating a short CUD, interhemispheric transfer is assumed to depend on non-callosal cross-midline connections that may be sensitive to the eccentricity of the visual stimulus [28]. The present finding of a longer duration of the CUD with a stimulus eccentricity of 8° compared with a stimulus eccentricity of 4° is generally compatible with this assumption. Corballis [19], among others, has argued that the critical pathway for interhemispheric communication of visual information following callosotomy is the commissure of the superior colliculi. There were no clinical or radiological signs of lesions to this commissure in patient OG, whose ocular mobility was intact.

A left ear suppression in verbal dichotic tests is a typical ID symptom exhibited by patients with total or near total callosal disconnections, and is regarded as evidence for a normal involvement of the corpus callosum in the transfer of verbal auditory information from the right hemisphere to the left for report [42,49]. Abnormalities in the performance of verbal dichotic tasks, stemming from a reduced processing of left ear inputs, have been noticed following closed head trauma and attributed to the encroachment of brain damage upon the corpus callosum [2,14,37,57]. The localization of the callosal region containing the fibers that convey verbal auditory information from the left ear to the left hemisphere is controversial. On one hand, some previous findings in patients with surgical or spontaneous partial callosal lesions have suggested that left ear suppression is selectively due to the interruption of fibers in exactly the callosal region that appears permanently damaged in the patient OG [2,51]. On the other hand, a detailed analysis of the surgical partial callosal sections that cause a left ear suppression in verbal dichotic tests has suggested that the splenium, in addition to the posterior callosal trunk, must be injured for the occurrence of a permanent symptom [32,52]. The presence of a left ear suppression in a verbal dichotic test shortly after the trauma in OG is in obvious agreement with the studies that attribute left ear suppression to a presplenial lesion, while the disappearance of the symptom in later follow-up tests is compatible with the suggestion that auditory callosal fibers run in the splenium as well as in presplenial callosal portions. Anatomical findings in the cat demonstrate a spread of fibers from cortical auditory areas over the entire posterior half of the corpus callosum, where they are interspersed with interhemispheric connections of other cortical areas [17,40]. It seems therefore plausible that in OG, auditory callosal fibers running in the intact splenium may have compensated for the initial deficit caused by the injury to the auditory presplenial fibers. In agreement with this hypothesis, a recent study of left ear suppression in verbal dichotic listening tasks in patients with splenial and nonsplenial callosal lesions has suggested that auditory callosal fibers pass through the splenium more posteriorly than previously thought [45].

OG's deficient ability to name objects and read words in the left visual field, and to compare visual stimuli in the two hemifields, may be attributed to a dysfunction of splenial visual fibers, but unlike the prolonged CUD these deficits improved dramatically or disappeared with the passage of time, thus, attesting the recovery of a functional integrity by the splenium, at least as regards interhemispheric visual communication.

Attempts at establishing an anatomo-functional topography of the human corpus callosum are hampered by the absence of a precise knowledge of the position within the corpus callosum of contingents of fibers belonging to different cortical areas. The limited evidence that exists comes indirectly from analyses of partial callosal degenerations or

atrophies after neuronal losses in select neocortical areas [20,43], and does not clearly suggest that fibers with a specific function, or a specific cortical origin and destination, are channeled into a restricted sector of the human corpus callosum. In animals, studies in cats indicate that fibers from discrete parts of the cortex disperse through large portions of the corpus callosum, where they intermix with fibers with different cortical relations and functions [40]. In macaque monkeys, the majority of commissural fibers from a given cortical region tend to occupy a distinct location in the corpus callosum, but overlaps of callosal fibers from different cortical areas have also been noted in the body of the corpus callosum, suggesting that the anatomic segregation of functionally diversified contingents of callosal fibers is far from precise [44]. Current tentative functional maps of the human corpus callosum are mostly based on observed associations between discrete callosal lesions and specific behavioral deficits [22,27], but the systematicity of these associations is questionable. A widespread distribution in the corpus callosum of fibers serving different functions can obviously interfere with the emergence of clear-cut ID symptoms after relatively small callosal lesions. The apparent absence of all typical ID symptoms after large callosal lesions that spare the sole splenium [26], and the temporary character of some ID symptoms caused by partial callosal lesions, as described here and in other studies [33,46], are also difficult to reconcile with the hypothesis of a strict and unvarying functional parcellation of the corpus callosum. Perhaps it will be possible to arrive at a reliable functional map of the human corpus callosum only by a considerable increase in the number of observations of correlations between circumscribed callosal lesions and select ID symptoms, coupled with a more precise identification and qualification of hemispheric interaction deficits.

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