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"Interhemispheric integration of simple visuomotor responses in patients with partial callosal defects"

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Interhemispheric integration of simple visuomotor responses in patients with partial callosal defects

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Abstract

Because of the organization of visual and motor pathways, simple manual responses to a light stimulus in the right or left visual hemifields are performed faster with uncrossed hand-field combinations than with crossed hand-field combinations. Uncrossed responses can be integrated within a single hemisphere, whereas crossed responses require a time-consuming interhemispheric transfer via the corpus callosum which is reflected in the difference between crossed and uncrossed reaction times. We investigated crossed-uncrossed differences (CUDs) in speed of simple visuomotor responses to lateralized flashes in seven subjects with an anterior section of the corpus callosum sparing the splenium and in one subject with an agenetic absence of the splenium due to a cerebrovascular malformation. There was no evidence of an abnormal prolongation of the CUDs in any of these subjects, in sharp contrast with the very long CUDs exhibited by an epileptic subject with a complete callosal section and two subjects with total callosal agenesis tested in the same experimental situation [1]. The normality of the CUDs in the subjects with partial callosal defects was not due to a postoperatory reorganization of interhemispheric communication, since there was no indication of an increased CUD in a patient tested as early as 5 days after the anterior callosotomy. These results are compatible with the assumption that both anterior and posterior callosal routes may subserve the integration of speeded manual responses to a visual stimulus directed to the hemisphere ipsilateral to the responding hand.

Key words: Visuomotor integration; Interhemispheric communication; Callosotomy in man; Callosal agenesis; Reaction time

1. Introduction

Subjects with total callosal agenesis as well as epileptic patients submitted to a complete section of the corpus callosum show a typical deficit in simple visuomotor reaction time (RT) to unstructured visual stimuli. When normal subjects make a speeded manual key-pressing response to a flash of light presented in the right or left visual hemifield, their RT is faster if responding hand and visual stimulus are matched for side, i.e. right hand and right stimulus or left hand and left stimulus, than if they are not (e.g. [11,13,14,18,21,22,25,26,30,32,33,35,37]; for earlier studies see [5]). The difference in RT between crossed and uncrossed reactions (CUD) can be accounted for by the fact that each visual hemifield projects to, and each hand is under the motor control of, the opposite hemisphere. Thus, while uncrossed reactions can be directly mediated within the same hemisphere, crossed reactions require an extra time for communication between the hemisphere receiving the visual stimulus and that controlling the responding hand. Patients with callosal agenesis or total callosotomy can perform crossed visuomotor reactions, but they exhibit CUDs that are several times longer than the 2–3 ms CUDs ordinarily seen in normals, thus indicating that the corpus callosum is normally required for the fast integration of crossed visuomotor reactions [1,11,14,18,23,24,30,33].

Hypothetically, the corpus callosum may subserve the integration of crossed visuomotor reactions by transferring the visual input across the midline, or by transmitting a "go-signal" to premotor and motor areas of the hemisphere which emits the response [7]. If the transfer were purely visual, the CUD should be strongly affected by changing the intensity of the visual stimuli, or by presenting stimuli with equal intensities to retinal positions with different sensitivities. The fact that the CUD remains

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invariant across major changes in intensity and eccentricity of visual stimuli strongly suggests that the callosal transfer mediating crossed responses is not a replica of the visual input, but rather a trigger for the response [7,24,25]. This implies that the transfer normally occurs by way of non-visual callosal routes, perhaps through anterior and/or middle callosal portions interconnecting premotor and motor areas of the frontal lobes, a possibility which has been supported indirectly by the finding that the CUD is matched by interhemispheric differences in latencies of potentials evoked by lateralized visual stimuli at central, but not occipital sites [31]. However interhemispheric routes for the initiation of motor responses to visual stimuli may also run in the splenium of the corpus callosum along with purely visual interhemispheric pathways (see Discussion).

The question of which part of the corpus callosum is normally responsible for mediating speeded crossed reactions can be answered directly by measuring the CUDs of patients with sections restricted to different callosal portions. If a particular contingent of callosal fibers were selectively involved in the callosal transfer underlying this integration, then the abnormal increase in the CUD should be observed not only in the complete absence of the corpus callosum, but also after a partial callosal section interrupting the putative specific pathway. While CUDs have now been assessed in numerous patients with complete callosal agenesis or callosotomy [1,11,14,18,23,24,30,33], there is only one report of an abnormal CUD, as long as in complete callosotomy patients, in a single case with a section of the anterior and middle corpus callosum sparing the splenium [14]. A confirmation of this finding in a larger group of patients with similar callosal lesions would provide strong support to the notion that the interhemispheric transfer underlying crossed reactions occurs in the anterior and/or middle corpus callosum.

The present study was undertaken to examine the interhemispheric integration of simple visuomotor responses in seven epileptic patients with surgical sections of the anterior and middle corpus callosum. The CUDs of these patients were compared with the CUDs of subjects totally lacking the corpus callosum. In addition, we tested the hypothesis of a possible involvement of the splenium in the integration of crossed visuomotor reactions by measuring the CUD of a non-epileptic patient with a large posterior callosal defect due to a vascular malformation. Part of the results have been preliminarly published as an abstract [36].

2. Materials and methods

Subjects. Seven epileptic patients and one non-epileptic patient with an intracerebral arterovenous (AV) malformation gave their informed consent to participate in this study. The first seven patients (B.S., C.G., F.P, G.V., G.E., I.D)., V.G.) had been suffering for several years from drug-resistant forms of idiopathic epilepsy, and had been submitted to section of the anterior and middle corpus callosum at the Institute of Neurosurgery of the Catholic University in Rome in an effort to reduce the severity of their condition. Objective assessments based on magnetic resonance imaging (MRI) show that the extent of the callosal section varies from the anterior third to the anterior four fifths of the corpus callosum, the splenium being spared in all cases. Sagittal MRI views of the brain of five of these patients, showing the consistent sparing of the splenium, are presented in Fig. 1. The completeness of the intended callosal sections was confirmed on coronal MRI images by experienced radiologists. The extent of the sections in patients B.S. and G.V. was evaluated at operation by the neurosurgeon to include the anterior one third and four fifths, respectively, of the corpus callosum, again sparing the splenium. The non-epileptic patient (Z.A.), whose sagittal MRI is also included in Fig. 1, was recruited at the Neurosurgical Department of the General Hospital of Verona where she had been examined for symptoms of increased intracranial pressure due to bleeding from an arterovenous (AV) malformation, followed by spontaneous regression in a few days. She has been diagnosed by experienced neuroradiologists to have an agenetic absence of the posterior third of the corpus callosum, including the splenium, due to her AV malformation. This is a medium-sized vascular structure (about 13 cc) which occupies the site of the missing posterior third and splenium of the corpus callosum, see Fig. 1. The AV malformation appears to be fed by both the anterior and posterior cerebral arteries and to drain into an enlarged varicose tributary of the great cerebral vein of Galen.

Essential clinical data for all patients are summarized in Table 1; see [27a] for more detailed descriptions of their pathological conditions as well as about the general outcome of the surgical treatment.

All epileptic patients except G.V. were tested at the Institute of Human Physiology of the University of Verona at least 1 month, and usually several months after callosotomy (see Table 1). The patient with the vascular malformation was also tested at the same Institute, 3.5 months after admission to the Hospital. Patient G.V. was tested at the Institute of Neurosurgery of the Catholic University in Rome both before and shortly after callosotomy for comparing her preoperative CUD with her short-term postoperative CUD so as to assess immediate effects of partial interhemispheric disconnection on visuomotor integration.

Controls. Data from the above patients could be directly compared with those from another epileptic subject (M.E.)

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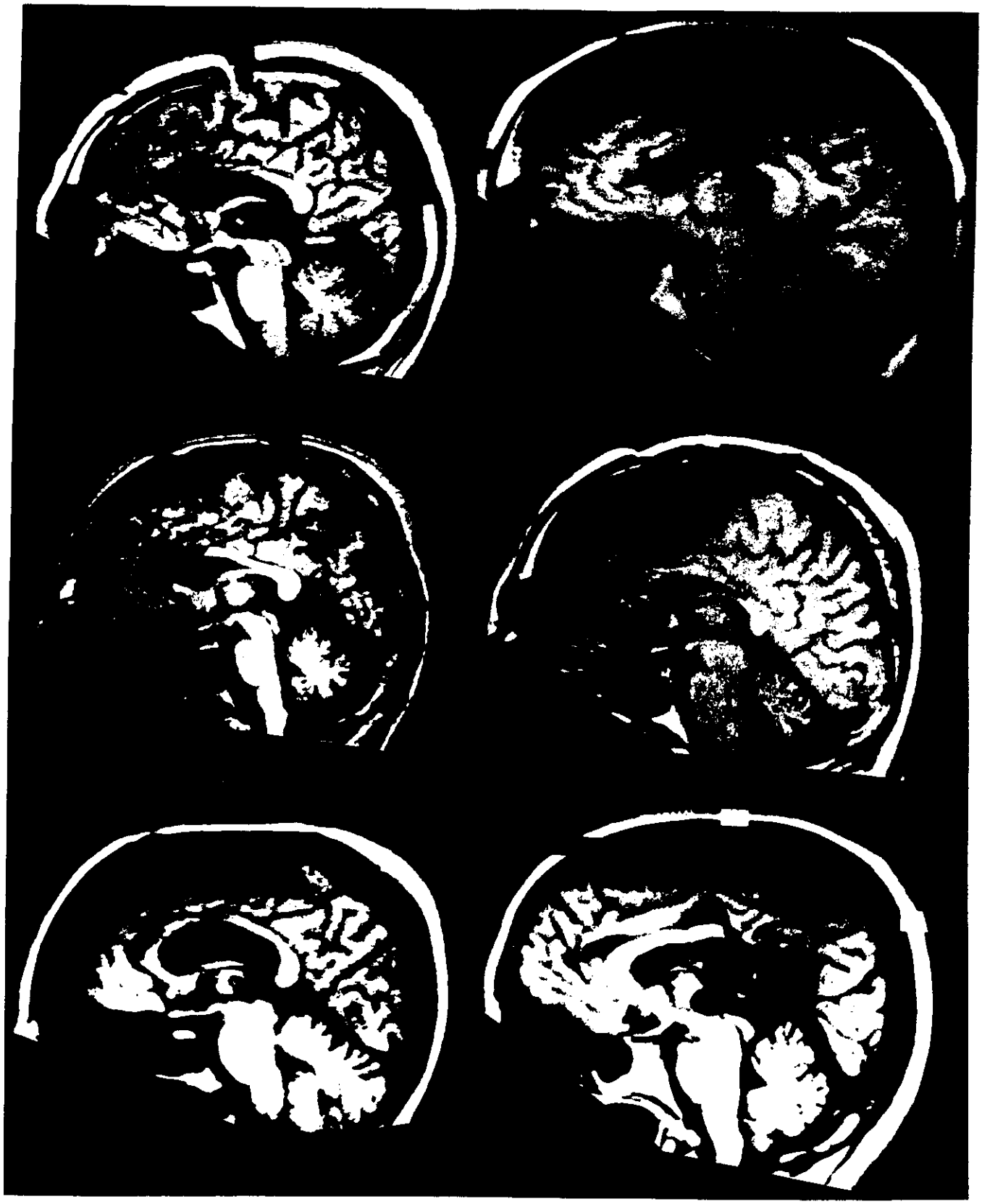

Fig. 1. MRI sagittal view of the brain of callosotomy patients C.G. (top left), F.P. (top right), G.E. (middle left), I.D. (middle right), V.G. (bottom left) and of patient Z.A. with an intracerebral AV malformation (bottom right). The anterior callosal section is most extensive in I.D. and least extensive in G.E.

Table 1
Demographic and clinical features

Patient	Age*	Sex	Education #	Date of operation	Minimum operation-test interval @	Laterality index ^	Drug therapy	MRI signs of brain pathology (callosal defects excluded)
B.S.	29	F	8	July '86	3 y 5 m	16	CBZ + PB	none
C.G.	22	M	15	Dec '90	1 y 7 m	22	CBZ + PB	bilateral dysplasias in occipital cortex
F.P.	22	F	8	May '89	11 m	19	CBZ + PB	bilateral temporoparietal pachigyria
G.V.	34	F	5	Apr '91	5 d	24	CBZ + PB + others	bilateral parietal pachigyria
G.E.	25	M	11	Dec '87	1 y 9 m	24	CBZ + PB + others	none
I.D.	21	M	8	May '90	6 m	24	CBZ + PB	none
V.G.	40	F	5	May '90	1 m	22	CBZ + PB + others	bilateral heterotopic islands of grey matter in periventricular region and parietal dysplasias
Z.A.	50	F	5			24	none	intracerebral AV malformation

* Age is given at operation time for all patients except Z.A. whose age is given at testing time; # in years of schooling; @ d = days; m = months; y = years; ^ according to Briggs and Nebes [9]. Subjects with scores between 9 and 24 are considered right-handed. CBZ = carbamazepine; PB = phenobarbital.

who had undergone complete callosotomy at the Institute of Neurosurgery of the Catholic University in Rome, and two subjects with complete callosal agenesis (R.B., P.M.). These three subjects had been tested in the Institute of Human Physiology of Verona with the same apparatus and in the same experimental conditions as used with the patients with partial callosal defects, as reported in detail elsewhere [1].

Apparatus. Testing in Verona was carried out in a partially sound-proofed cubicle where the subject sat facing an arc perimeter 57 cm in radius attached to a white screen. The screen and the perimeter were illuminated from above at a luminance of 0.15 cd/m^2. The patient positioned his/her head in a forehead- and chin-rest located at the center of curvature of the perimeter. Two solid state miniature bulbs (TIL 222) were fastened to the perimeter, one on the left and the other on the right of a central mark for fixation. From the patient's viewpoint, the visual angle subtended by each bulb was half a degree, and the angular distance between the fixation mark and the bulb on each side could be 10, 35 or 70 degrees, as specified later. Each bulb could be lighted individually by a square pulse of current, producing a gallium phosphide green flash with a 5 ms duration and an intensity of about 1000 μcd. Two button-keys, one on each side of the subject, were used as response devices. Each of them was fastened to the top of a brass cylinder. Subjects prepared to operate these response devices by clutching the cylinder with the whole hand and by positioning the tip of the thumb on the button-key; the actual response consisted in pressing the key by flexing the thumb. During testing, patients wore a headset which delivered a standard auditory warning signal. Testing of patient G.V. in Rome was carried out with an AT 80286 personal computer provided with an IBM color monitor and a medium resolution VGA graphic interface. By positioning the head on a chin-rest the patient looked at a fixation mark in the center of the screen from a distance of 30 cm; the visual stimulus was a white rectangle, with base equal to 0.5 cm and height equal to 0.8 cm, which was flashed for 16.6 ms at a distance of 3 cm (i.e. 5.7 degrees) to the right or left of the fixation mark. The background luminance was 0.1 cd/m^2, and that of the stimulus was about 60 cd/m^2. The computer was also programmed to generate through a loudspeaker a warning auditory signal. The onset of the visual stimulus started a ms counter which could be stopped by pressing the space bar of the computer's keyboard.

Procedure. In Verona, subjects were first accustomed to the experimental situation by running several practice trials, and then underwent formal testing over two or more days during repeated sessions including and separated by rest periods commensurate with individual fatigability. Each session consisted of one or more blocks of 30 or 50 trials; each trial involved a sequence of a warning auditory signal delivered via the headphone set, followed after an interval varying randomly between 1 and 3 s by a flash in the right or left visual hemifield. According to a simple RT paradigm, in any block patients were to press a given key

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as soon as possible after seeing the light flash, regardless of whether it occurred in the right or left hemifield. They were also instructed to fixate on the central mark upon hearing the warning signal and to maintain fixation until after pressing the appropriate key. Eye position and maintenance of fixation were monitored by television, and trials with failures to fixate were aborted and repeated. On each trial the time elapsing between flash onset and keypressing response was electronically measured to the nearest millisecond. The presentation of the flashes and the recording of the RT data were automatically controlled by a computer which rejected RTs shorter than 150 ms or longer than 989 ms, and replaced the rejected trials later in the sequence.

Subjects B.S., C.G., F.P., G.E., and V.G. were tested according to an experimental design which required the completion of 12 blocks of 50 trials. Flashes could be presented at 10, 35 and 70 degrees of visual angle from the fixation point along the horizontal meridian in either hemifield; however the eccentricity of flash location was held constant in each of the 12 blocks. Six blocks were allocated to a condition called random, in which on any trial the flash could occur in either visual hemifield; and 6 blocks were allocated to a condition called blocked, in which flash location was the same in each half-block. In each block of the random condition, flash location alternated unpredictably and equiprobably between hemifields, yielding 25 stimuli per hemifield per block. Two blocks were allocated to each of the three flash eccentricities, and with each flash eccentricity one block was performed responding with the right hand and the other responding with the left hand. In the blocked condition, two blocks were again allocated to each of the three flash eccentricities, one block for the right hand and the other for the left hand. In each block, the flash appeared constantly in one hemifield on the first 25 trials and in the other hemifield on the remaining 25 trials. In the blocked condition the subject was informed about the hemifield in which the flash would appear both before the beginning of each block and before the beginning of the 26th trial. In each patient, alternations between different eccentricities, hands, hemifields and conditions were effected according to a Latin square design. In addition to the above 12 blocks, G.E. completed 6 more 50-trial blocks in the random condition, 2 of which were allocated to each of the 3 flash eccentricities; for each eccentricity, one block was run using the right hand and the other using the left hand. V.G. also completed 4 additional 50-trial blocks, 2 for the right hand and 2 for the left hand, the condition being random and the flash eccentricity being 10 degrees from fixation.

Subjects I.D. and Z.A. were tested only with a 10-degree flash eccentricity and only in the random condition. Fewer trials were run with these subjects than with the previous ones because they were submitted to other tests that will be reported elsewhere. They completed 4 30-trial blocks, 2 of which were run responding with the right hand and 2 with the left hand. The alternation between right-hand blocks and left-hand blocks varied from subject to subject and was balanced across subjects according to a Latin square design.

In Rome, patient G.V. was tested during one preoperative session, 4 days before callosotomy, and one postoperative session, 5 days following callosotomy. Being affected by a severe divergent strabismus which prevented binocular fixation, she was tested with one eye occluded by a patch. Each of the two sessions included 8 blocks, each of which consisted of 30 trials. Each trial involved the delivery of the warning auditory signal followed, after an interval varying randomly between 1 and 3 s, by the visual stimulus, which was to be reacted to as fast as possible by pressing the space bar of the computer's keyboard with an index finger. Milner et al. [26] have shown that CUDs assessed with this type of response do not differ from those assessed with responses consisting in discrete movements of the thumb. The location of the visual stimulus varied randomly from right to left from trial to trial, subject to the constraint that in each block there was an equal number of right and left stimuli. In each session, 4 blocks were performed using the right eye and 4 blocks were performed using the left eye; further, the patient used the right hand for responding in 2 right-eye blocks and 2 left-eye blocks, and the left hand for responding in the other blocks. In each session the alternations between hands and eyes were performed according to a balanced design. Fixation was controlled by an experimenter sitting behind the computer; trials with defective fixation and/or RTs shorter than 150 ms or longer than 900 ms were discarded and replaced later in the sequence.

3. Results

Clinical signs of interhemispheric disconnection. Typical signs of interhemispheric disconnection in right-handed patients, such as left-hand anomia, left-hand apraxia on verbal command, and left-hemifield alexia [8,29,34], were generally absent at the time of the CUD assessments in our partial callosotomy patients, all of whom have a spared splenium (Fig. 1). The only notable exception was an impaired intermanual transfer of localization of tactile stimuli to the fingers in patients G.E. and I.D. This symptom has been reported in some patients with lesions of the trunk of the corpus callosum [6,10,16], but not in others [17]. This variability may be due to differences in the testing methods or in the individual organization of the callosal connections. At the time of her CUD assessment, patient

Z.A., lacking the posterior third of the corpus callosum, showed a deficient intermanual transfer of tactile discrimination as well as left-hand anomia and left-hemifield alexia.

RD data. The occurrence of errors of fixation and anticipations was negligible in all patients. The number of omissions varied considerably from patient to patient, ranging from 1% to 9%, but they were evenly distributed across hemifield/hand combinations in all patients. Patients under pharmacological antiepileptic treatment usually produce abnormally long RTs with a high variance. Since this was true also in the present study, RT variance was reduced by excluding RTs above 700 ms from analysis. (This cutoff criterion was adopted a posteriori rather than during testing because the automatic replacement procedure would have made testing unbearably long for at least some of the patients). A preliminary analysis of the data by analysis of variance (ANOVA) showed that stimulus eccentricity and type of stimulus presentation (blocked vs random) had no systematic effect on the CUD, both within and across subjects. Therefore the RTs of subjects B.S., C.G., F.P., G.E. and V.G., who had been tested with different stimulus eccentricities and different types of stimulus presentation, were conflated across these variables. For subjects G.E. and V.G. the conflation included the RTs of the extra blocks run in addition to those of the regular experimental design. Table 2 shows RT as a function of side of stimulus and responding hand as well as the overall CUD for each subject. Individual CUDs were computed by subtracting mean RT of uncrossed combinations from mean RT of

Table 2
The Table gives (1) mean RT (± S.E.M.) for each hemifield/hand combination for each experimental subject as well as for the three subjects totally lacking the corpus callosum; and (2) the corresponding CUDs

Patients with partial callosal defects

Subject	Uncrossed RTs (ms)			Crossed RTs (ms)			CUD (ms)
	LF-LH	RF-RH	Mean	LF-RH	RF-LH	Mean	
B.S.	493.2 ± 8.6 (134/150)	503.9 ± 7.5 (130/150)	498.5	519.4 ± 7.4 (122/150)	491.6 ± 8.2 (134/150)	505.5	7
C.G.	350.0 ± 6.0 (150/150)	354.4 ± 5.4 (150/150)	352.2	346.3 ± 4.7 (149/150)	387.2 ± 6.6 (148/150)	366.7	14.5
F.P.	385.9 ± 5.1 (145/150)	370.8 ± 7.8 (150/150)	378.3	357.3 ± 5.7 (150/150)	394.0 ± 7.0 (145/150)	375.6	− 2.7
G.V. pre	394.2 ± 8.3 (60/60)	402.8 ± 12.2 (60/60)	398.5	409.8 ± 10.3 (60/60)	403.3 ± 9.2 (60/60)	406.5	8
post	563.5 ± 13.8 (33/60)	537.5 ± 17.1 (44/60)	550.5	546.2 ± 14.2 (45/60)	538.7 ± 16.6 (38/60)	542.5	− 8
G.E.	350.5 ± 6.2 (223/225	284.0 ± 4.5 (225/225)	317.2	305.8 ± 5.6 (224/225)	327.2 ± 5.6 (221/225)	316.5	− 0.7
I.D.	332.7 ± 17.4 (30/30)	272.7 ± 16.4 (29/30)	302.7	313.2 ± 13.9 (30/30)	301.5 ± 10.6 (29/30)	307.3	4.6
V.G.	493.2 ± 7.5 (177/200)	516.8 ± 7.6 (174/200)	505	494.2 ± 7.4 (186/200)	510.4 ± 7.8 (177/200)	502.3	− 2.7
Z.A.	275.2 ± 6.9 (30/30)	266.7 ± 6.0 (30/30)	270.9	277.7 ± 7.3 (30/30)	287.8 ± 14.3 (30/30)	282.7	11.8

Patients with total callosal defects

Subject	Uncrossed RTs (ms)			Crossed RT (ms)			CUD (ms)
	LF-LH	RF-RH	Mean	LF-RH	RF-LH	Mean	
M.E. (total section	405.4 ± 12.6 (112/150)	300.7 ± 6.5 (150/150)	353.1	486.1 ± 11.1 (113/150)	386.4 ± 7.9 (146/150)	436.3	83.2
R.B. (callosal agenesis)	275.6 ± 9.1 (30/30)	307.8 ± 13.4 (30/30)	292.1	320.4 ± 8.2 (30/30)	308.8 ± 9.2 (30/30)	314.6	22.5
P.M. (callosal agenesis)	238.9 ± 9.8 (15/15)	229.3 ± 7.9 (15/15)	234.1	264.8 ± 8.3 (15/15)	254.3 ± 6.0 (15/15)	259.5	25.4

In brackets: number of RTs accepted for the analysis out of the total valid RT. LF = left visual hemifield; RF = right visual hemifield; LH = left hand; RH = right hand. "Pre" and "post" for subject G.V. refer to data obtained before and after acute callosotomy. The high cut-off of RTs analyzed for each patient was set at 700 ms.

crossed combinations: these uncrossed and crossed RT means also appear in Table 2. (Means rather than medians were used as measures of central tendencies in order to facilitate comparisons with previous studies on CUDs in callosotomized subjects, also expressed as differences between means [1,11,33]). Further, Table 2 shows the number of RTs analyzed for each hemifield/hand combination in each subject, indicating that differences between RT frequencies for different combinations were non-existing or minimal and clearly non-systematic. The results from each individual were subjected to separate ANOVAs for completely randomized designs with unequal cell frequencies and unweighted means using data from individual trials as the random-effect variable [27]. In all subjects except G.V. these ANOVAs had two fixed-effect variables (hand and hemifield), while in the ANOVA for G.V. there was one additional fixed variable, i.e. operation (with levels pre and post). Most subjects showed significant differences between the hands and/or the hemifields. The right hand was significantly faster than the left hand in C.G., F.P. and G.E. and the left hand was significantly faster in B.S. The right hemifield yielded faster RTs than the left in G.E. and I.D, while the left hemifield yielded faster RTs than the right in C.G. and V.G. The differences between hands and/or hemifield may reflect a prevalent damage to one hemisphere (including functional damage from surgical manipulations), particularly in those cases exhibiting long RTs for the hand and the hemifield of one side (see Table 2), since usually these long RTs do not occur in normal subjects tested in the same way (e.g. [13,37]). In no subject except C.G. did the hand/hemifield interaction approach significance, supporting the conclusion that individual RT did not depend systematically on the relation between side of stimulus and responding hand. C.G., the only anterior callosotomy patient whose data yielded a significant hand/hemifield interaction in the ANOVA ($P<0.01$), showed a significant overall difference between uncrossed and crossed RTs on a t-test for unpaired scores ($P<0.01$). Yet, although his CUD of 14.5 ms was the largest among those of our patients with partial callosal defects, including Z.A., it was substantially smaller than those found in the same experimental conditions in one subject with complete callosotomy (83.2 ms, M.E.) and two subjects with complete callosal agenesis (22.5 ms, R.B. and 24.5 ms, P.M., see Table 2). Further, contrary to the completely acallosal subjects, in whom uncrossed RTs are consistently faster than crossed RTs in either visual hemifield, the superiority of uncrossed over crossed RTs was limited to the right visual hemifield of C.G. (see Table 2). Patient Z.A., affected by an agenetic absence of the splenium, also showed a relatively large CUD of 11.8 ms, but the hand/hemifield interaction was far from significant in the ANOVA on her data. In patient G.V. the ANOVA revealed a significant effect of operation, postoperative RTs being longer than preoperative RTs ($P<0.001$). As shown in Table 2, the preoperative CUD of this patient was 8.0 ms, a value which falls within the range found with large series of normal subjects (e.g. [2,35]), while the postoperative CUD was −8.0 ms. Negative CUDs can be seen in a minority of normal subjects, and are usually interpreted as errors of measurement; however, in the case of G.V. the postoperative CUD negativity most probably depended on the fact that the left-hemifield/left-hand RT was much more affected than the RTs for the other combinations by the generalized postoperative slowing. This left side decrement in performance found in the acute state after callosotomy seems best attributed to a dysfunction of the right hemisphere which was retracted during the operation.

The grand mean of the CUDs across the 6 callosotomy patients tested at least one month after surgery was equal to 3.3 ms ($\pm$ 2.8 ms, S.E.M.). This value can be compared with grand CUD means of 7.4 $\pm$ 1.9 ms, 2.2 $\pm$ 0.4 ms, and 2.7 $\pm$ 1.3 ms found in 48, 12 and 8 normal subjects tested with the same apparatus [2,13,37]. The grand CUD means in those groups of normal subjects were all significantly different from 0, since within each group uncrossed RTs were significantly faster than crossed RTs. By contrast, the grand mean of the CUDs in the six chronic callosotomized patients, though quantitatively comparable to normal values, did not differ significantly from 0 on a one-sample t-test because as many as three of these six patients had slightly negative CUDs. As already discussed, these negative CUDs may be errors of measurement, or they may result from a hemispheric dysfunction affecting the contralateral hand and hemifield and the related uncrossed RT. The latter possibility is suggested by the fact that as in G.V. (see above), in two of the three chronic callosotomy patients with negative CUDs (G.E., V.G.) one of the ipsilateral combinations did in fact yield the slowest RT, an event which does not occur in normal groups [22].

4. Discussion

Concordant findings from different laboratories support the notion that an abnormally long CUD is a reliable and consistent marker of a total absence of the corpus callosum, whether congenital or acquired [1,11,14,18,23,24,30,33]. The demonstration of a normal CUD in patients with partial callosal lesions or sections should thus be taken to indicate that the remaining callosal portions suffice for the fast integration of crossed reactions. Our findings do not support the expectation of an abnormal prolongation of the CUD in patients with anterior callosotomies, because there was no evidence for this prolongation in at least six

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of our anterior callosotomy patients. A CUD prolongation in these patients cannot have been masked by the large variances of their individual RTs. The abnormally long CUDs reported in the literature have indeed been observed in patients with complete callosal agenesis or sections, who show RTs variabilities as great as or even greater than those described here for partial callosotomy patients [1,11,14,18,23,24,30,33]. Further, since there was no evidence for a prolonged CUD in the patient tested 5 days after the operation, a postoperative reorganization of interhemispheric communication is unlikely to account for the short CUDs of these patients, unless one assumes an extremely rapid functional change in the remaining portions of the corpus callosum.

We therefore believe that interhemispheric connections running in the posterior corpus callosum of these patients can ensure by themselves a normal speed of crossed reactions. The absence of abnormally long CUDs in our group of anterior callosotomy patients would seem to outweigh the opposite evidence of an abnormal CUD in a single case with a similar splenium-sparing anterior callosotomy [14]. The CUD of this patient fell within the range of the extremely long CUDs of complete callosotomy patients [1,11,33]. The reasons for the discrepancy between the present findings and those of Di Stefano et al. [14] are unclear. One possibility is that the splenium of their patient, though seemingly preserved at the MRI examination, may in fact be only partially functional because of damage undergone during an intended attempt to perform a complete callosotomy [19]. In this connection it is noteworthy that our patient C.G., in whom there was a hint of a slightly increased CUD, may have abnormal callosal connections through the splenium because of pronounced dysplasic cortical malformations in the occipital regions of both sides (see Table 1).

The suggestion that the information for the fast integration of crossed reactions in our anterior callosotomy patients is tranferred by posterior callosal connections does not necessarily imply a visual character of this information. The available evidence on callosal topography in man indicates that the splenium contains not only the callosal connections of visual areas in the occipital lobes, but also those of the posterior-inferior parietal cortex [12]. This part of the parietal lobe includes cortical areas which appear to be important for the initiation of oculomotor and skeletomotor responses to visual stimuli [3], and very long CUDs have been reported in patients with parietal lesions [4]. It is conceivable that parietal regions with callosal connections running in the splenium have a role in coordinating motor initiation functions across the hemispheres.

Anyhow we cannot conclude from our data that crossed visuomotor reactions are normally integrated across the midline via posterior portions of the corpus callosum, since there was no noticeable prolongation of the CUD also in patient Z.A., who had an agenetic defect of the entire splenium. The intracerebral AV malformation in this patient is thought to involve the persistence of embryonic vessels pre-existing to the development of the corpus callosum [28], and to have blocked the normal formation of the splenium. Data from this patient must be interpreted with caution because the topographic organization of her incompletely developed corpus callosum may be abnormal. For example, the anterior portions of her corpus callosum may contain at least part of the fibers that would normally run in the splenium. This possibility does not seem very likely, given that she exhibited clear signs of visual and tactile interhemispheric disconnection. At any rate, a direct test of the importance of the splenium for the integration of speeded crossed visuomotor reactions would seem to require an assessment of the CUD in patients with callosal defects restricted to the splenium. Until this evidence becomes available, it cannot be stated with certainty whether or not the integrity of the anterior part of the callosum can ensure by itself the normality of the CUD.

At the moment, two possibilities suggest themselves. One possibility is that the interhemispheric integration of simple visuomotor responses can be coordinated by virtually all portions of the corpus callosum. This possibility has been suggested to apply to the interhemispheric integration of visually guided reaching in monkeys [20]. The other possibility is that posterior callosal routes are more important than anterior ones for interhemispheric visuomotor integration. This antero-posterior difference has been substantiated in relation to deficits of visuomotor praxis in patients with complete and partial callosotomies. Complete callosotomy patients are unable to imitate with one hand finger postures visually presented to the hemifield contralateral to the performing hand [15]. This deficit, which is accounted for by the disconnection between the hemisphere controlling the response and the hemisphere receiving the visual input [15], çan be observed also after sections limited to the posterior corpus callosum, but not after anterior callosotomies [39]. It remains to be determined whether the callosal substrates for the integration of speeded crossed visuomotor reactions are related to those mediating visually guided reaching, or to those involved in the more complex task of visuomotor imitation of finger postures.

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