

Channels of the corpus callosum

Evidence from simple reaction times to lateralized flashes in the normal and the split brain

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Summary

We studied 75 normal subjects and three commissurotomed patients using unimanual simple reaction times to lateralized flashes as a behavioural estimate of interhemispheric transmission time. Three different versions of the paradigm were performed: (i) the basic task; (ii) a motor task, with an increased complexity of the motor response; and (iii) a visual task, with an increased complexity of the visual stimulus presentation. We tested two hypotheses. First, that the new versions of the simple reaction time task result in shifts in hemispheric specialization for processing motor output (indicated by a main effect of response hand) or visual input (indicated by a main effect of visual field) alone, without affecting callosal transmission. In that case normals and

split brain patients would show no significant task by response hand by visual field interaction and no significant task by crossed–uncrossed difference interaction. Secondly, that the new versions of the task affect callosal transfer. In that case, normals, but not split brain patients, would show a significant task by response hand by visual field interaction and a significant task by crossed–uncrossed difference interaction. Results are consistent with the latter hypothesis, showing that the motor task significantly changed the response hand by visual field interaction and the crossed–uncrossed difference, but only in normal subjects, perhaps producing a switch in the callosal channel subserving the interhemispheric transfer.

Keywords: corpus callosum; interhemispheric transmission time; split brain

Introduction

Since 1912, Poffenberger's simple reaction time paradigm has been used to estimate interhemispheric transmission time in the normal brain. Here, unpatterned light flashes appear either in the right or the left visual half fields (LVF or RVF) and subjects are required to detect them by pressing a button either with the left or right hand (Lh or Rh). When the same hemisphere receives the visual input and controls the motor response (uncrossed conditions) there is no need for callosal transfer and response times are faster than when opposite hemispheres receive the input and control the response so that callosal transfer is necessary (crossed conditions).

When we subtract the two uncrossed from the two crossed conditions and divide by two, we get an estimate of average interhemispheric transmission time. This difference is usually ~3–4 ms in normal subjects (Marzi *et al.*, 1991). Subjects with agenesis of the corpus callosum have a conspicuously larger interhemispheric transmission time of ~15 ms, presumably mediated by the anterior commissure or by

subcortical pathways (Milner *et al.*, 1985). Patients with complete cerebral commissurotomy have an even larger interhemispheric transmission time of ~60 ms (Clarke and Zaidel, 1989; and *see* review in Marzi *et al.*, 1991). Clarke and Zaidel (1989) suggested that interhemispheric transfer can simultaneously occur through multiple pathways, both callosal and subcortical, and that the fastest pathway (the one that completes the interhemispheric transfer first) controls behaviour, horse-race fashion. Thus, short transmission time in presence of an intact corpus callosum (as in normal subjects) and long transmission time in absence of an intact corpus callosum (as in subjects with agenesis of the corpus callosum or commissurotomed patients) suggest that the callosal pathway is the fastest one.

The human corpus callosum can be viewed as a set of communication channels, each interconnecting different cortical regions and each with its own transfer properties, defined among others by the size, type and density of fibres

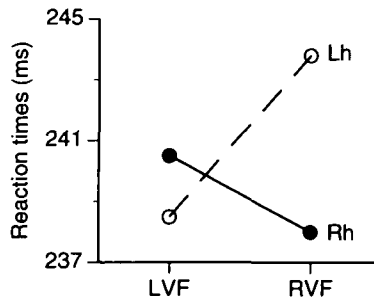


Fig. 1 Overall visual field by response hand interaction of a meta-analysis on simple reaction times to lateralized flashes (Marzi *et al.*, 1991).

in it (Zaidel *et al.*, 1990; Kennedy *et al.*, 1991; Aboitiz *et al.*, 1992). Thus, interhemispheric transfer can occur simultaneously through both motor and visual channels. It can be argued that if transfer is motor then it should be sensitive to motor parameters but not to visual ones, whereas if it is visual then it should be sensitive to visual parameters but not to motor ones (Berlucchi *et al.*, 1971). Using this logic, it is now generally believed that motor transfer dominates in the simple reaction time paradigm because manipulation of the visual brightness and eccentricity of the targets affects overall reaction time but does not affect interhemispheric transmission time in normal subjects (Berlucchi *et al.*, 1971; Clarke and Zaidel, 1989). Similarly, patients suffering from a motor deficit as a result of unilateral anterior cortical lesions show a longer transmission time compared with patients who have unilateral cortical lesions in similar areas but without motor symptoms (Vallar *et al.*, 1988). If the effective interhemispheric transfer is indeed motor, then we should be able to modulate it with manipulation of the motor programming component of the task. This was one of the goals of the present experiment and we attempted it using an alternating finger response paradigm, where subsequent trials require responses, in turn, by the index and middle fingers of the same hand.

In their meta-analysis of simple reaction time experiments, Marzi *et al.* (1991) noticed that the two crossed conditions, LVF-Rh and RVF-Lh, were unbalanced, the RVF-Lh condition being slower than the other one (Fig. 1). Further, there was an overall LVF advantage and an overall Rh advantage. They interpreted this as showing either that there is asymmetric callosal transfer, with faster right hemisphere-to-left hemisphere relay than left hemisphere-to-right hemisphere relay, or else that there is right hemisphere specialization for the visual components of the task and left hemisphere superiority in manual response. We believe that the two hypotheses are not mutually exclusive. We can schematize the information processing sequence from sensory registration to motor response and estimate the response times in the four possible experimental visual fields by response hand conditions as follows:

- (i) LVF-Lh: $V_R + P_R + M_R$ (uncrossed)
- (ii) LVF-Rh: $V_R + P_R + CR_{RL} + M_L$ (crossed)

- (iii) RVF-Rh: $V_L + P_L + M_L$ (uncrossed)
- (iv) RVF-Lh: $V_L + P_L + CR_{LR} + M_R$ (crossed),

where V_R is the latency of visual registration in the right hemisphere (LVF), V_L is the latency of visual registration in the left hemisphere (RVF), P_L is the latency of stimulus detection in the left hemisphere, P_R is the latency of stimulus detection in the right hemisphere, M_R is the latency of motor response with the Lh (right hemisphere), M_L is the latency of motor response with the Rh (left hemisphere), CR_{RL} is the latency of callosal relay from the right hemisphere to the left hemisphere, and CR_{LR} is the latency of callosal relay from the left hemisphere to the right hemisphere. We can incorporate next the hemispheric contributions to visual registration and stimulus detection into one component designated V , assuming as we do that the same hemisphere that receives the visual stimulus makes the detection. Then equations (i)–(iv) simplify into:

- (i') LVF-Lh: $V_R + M_R$ (uncrossed)
- (ii') LVF-Rh: $V_R + CR_{RL} + M_L$ (crossed)
- (iii') RVF-Rh: $V_L + M_L$ (uncrossed)
- (iv') RVF-Lh: $V_L + CR_{LR} + M_R$ (crossed)

From these equations we can get:

- (v) $LVF - RVF = [i'] + [ii'] - [iii'] - [iv'] = 2(V_R + V_L) + (CR_{RL} - CR_{LR})$
- (vi) $Lh - Rh = [i'] + [iv'] - [ii'] - [iii'] = 2(M_R - M_L) + (CR_{LR} - CR_{RL})$
- (vii) uncrossed difference = $[i'] - [iii'] = (V_R - V_L) + (M_R - M_L)$
- (viii) crossed difference = $[ii'] - [iv'] = (V_R - V_L) + (CR_{RL} - CR_{LR}) + (M_L - M_R)$

From Marzi *et al.*'s (1991) meta-analysis we know that $[v] < 0$, $[vi] > 0$, $[vii] = 0$, and $[viii] < 0$. This combination of results actually makes it possible to have asymmetries in callosal relay, stimulus processing and motor response simultaneously. In fact, if $CR_{RL} < CR_{LR}$, then it is possible to have simultaneously $M_L > M_R$ and $V_R < V_L$.

An indirect way to tease apart the contribution of each asymmetry to the final result showed by the meta-analysis, is to compare the pattern of the four visual field by response hand combinations in different populations. For example, if the crossed difference indeed shows that callosal relay from right hemisphere to left hemisphere is faster than relay from left hemisphere to right hemisphere, as argued by Marzi *et al.* (1991), then the asymmetry is apparently present in children and it is absent in split brain patients and in cases with callosal agenesis, suggesting that it is callosal in origin (Marzi *et al.*, 1991). Visual evoked potential data also support the hypothesis of asymmetric transmission time through the corpus callosum (Saron and Davidson, 1989; Brown *et al.*, 1994).

To test this hypothesis further, we introduced two new versions of the Poffenberger paradigm. In one, already mentioned, we increased the complexity of the motor

component by requiring alternating finger responses. We shall refer to this version as the 'motor task'. In the other, we increased the complexity of the visual search by introducing spatial uncertainty into the location of the flash. We shall refer to that version as the 'visual task'. The question is whether these task manipulations will affect the hemispheric contribution and/or the callosal contribution to the pattern of visual field by response hand interaction. Specifically, we predicted that a change in the hemispheric contribution would be indexed by an enlargement in visual field difference in the visual task and by an enlargement of response hand difference in the motor task in both normals and commissurotomed subjects (since callosal relay is not involved). We also predicted that a callosal contribution would be indexed by a task by visual field by response hand interaction and by a task by crossed-uncrossed conditions interaction in normals but not in split brain patients (note that a change in callosal relay will affect the response hand by visual field interaction, i.e. a task by crossed-uncrossed interaction entails a task by response hand by visual field interaction. However, a change in the response hand by visual field interaction need not imply a change in callosal relay). Consequently, we included three split brain patients in our sample. Two had complete cerebral commissurotomy and one had callosotomy sparing the splenium. We reasoned that the motor and visual tasks may affect interhemispheric relay by changing the cortical locus of the decision and thus also the callosal channel involved in transfer. Thus, the patient with partial callosotomy sparing visual callosal fibres allowed us to tease apart the role of motor and visual channels in the change. Given that normal transfer seems to be faster via motor pathways, we may expect the motor task to affect callosal relay more readily than the visual task.

Methods

Subjects

Seventy-five UCLA undergraduate students participated in this experiment. All the subjects were strongly right-handed as determined by a handedness inventory and had no left-handed relatives. All subjects reported normal or corrected-to-normal vision in both eyes and no history or evidence of neurological insult.

Three commissurotomy patients were also tested. Two of them, a 40-year-old man (L.B.) and a 60-year-old woman (N.G.), underwent complete section of the corpus callosum, hippocampal and anterior commissure at age 13 years and age 30 years, respectively. Magnetic resonance imaging evidence of completeness of callosotomy in these subjects has been reported by Bogen *et al.* (1988). The third patient, D.W., is a 30-year-old right-handed man with a history of chronic seizures who had undergone partial commissurotomy sparing the splenium and few fibres of the rostrum of the corpus callosum. Clinical, surgical and radiological details are described elsewhere (Iacoboni *et al.*, 1994). Subjects and

patients gave informed consent for participation in the study in accordance with the UCLA Human Subjects Protection Committee.

Apparatus and procedure

Subjects were seated in a dimly lit room at a distance of 57 cm from a high resolution RGB colour monitor of a MacIntosh Quadra computer, with their chins in a chinrest and eyes aligned with the fixation cross in the middle of the screen. A computer software for MacIntosh, MacProbe, written by Steve Hunt, was used to present stimuli and to record responses. Stimuli consisted of black flashes on a grey background, lasted 50 ms, and were presented from 500 ms to 2500 ms after a warning tone of 1000 Hz lasting for 100 ms, either in the RVF or in LVF in a random but counterbalanced fashion. A response panel with two vertically aligned keys, the top one for the index finger and the bottom one for the middle finger, was placed at midline and used for manual responses. In each testing session normal subjects received 14 blocks of 40 trials each, whereas split brain patients received 12 blocks of 40 trials each. In each testing session, the use of the right or of the left hand for motor responses was counterbalanced across blocks. Subjects' and patients' eye movements were monitored during all the testing sessions and when eye movements occurred the trial was discarded.

Three different tasks were performed: (i) fixed stimulus location-fixed motor response (basic task); (ii) fixed stimulus location-alternating motor response (motor task); (iii) random stimulus location-fixed motor response (visual task). In the basic task, flashes were presented on the horizontal meridian at 4° of eccentricity from the fixation cross placed in the middle of the screen and responses were performed with the index finger only. In the motor task, flashes were also presented on the horizontal meridian at 4° of eccentricity from the fixation cross and subjects were instructed to carry out responses alternating between index finger on odd trials and middle finger on even trials. Presentation of stimuli in the right or in the left visual field was counterbalanced for odd and even trials. For counterbalancing purposes, when a response error occurred (e.g. middle finger used on an odd trial), the computer excluded that trial and added one similar trial more in the same block. In the visual task flashes were randomly presented in nine different locations (three imaginary 'rows' and three imaginary 'columns') in each visual field at 4°, 8° and 12° from the vertical meridian, and on the horizontal meridian, 8° above and 8° below the horizontal meridian. Responses were performed with the index finger only. Normal subjects performed only one task in one testing session (25 subjects per task), whereas commissurotomed patients received three separate testing sessions, one per task.

Data analysis

Data from normal subjects were submitted to analyses of variance (ANOVA) with medians of reaction times for each

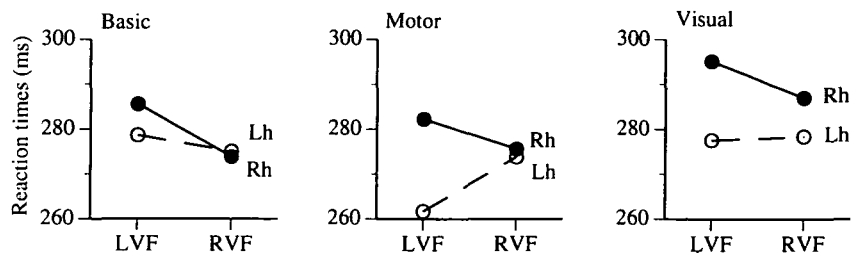


Fig. 3 Visual field by response hand interactions in D.W.

To further explore whether these differences in the response hand by visual field interaction between tasks actually reflected a significant change in interhemispheric transmission time we performed a 3 (task: basic, motor, visual) by 2 (condition: crossed, uncrossed) ANOVA, showing a main effect of condition, $F(1,72) = 53.8$, $P < 0.001$ (crossed = 255.7 ms; uncrossed = 252.7 ms), and a condition by task interaction, $F(2,72) = 6.3$, $P < 0.004$. A one-way ANOVA in each task showed that crossed and uncrossed conditions were significantly different in the basic task, $F(1,24) = 32.4$, $P < 0.001$ (crossed = 255.8 ms; uncrossed = 251.5 ms) and in the visual task, $F(1,24) = 24.9$, $P < 0.001$ (crossed = 262.5 ms; uncrossed = 258.9 ms), but not in the motor task $F(1,24) = 2.6$, $P > 0.05$ (crossed = 248.7 ms; uncrossed = 247.7 ms).

Commissurotomed subjects

Split brain patients have shown a large variability in reaction times and interhemispheric transmission time in previous experiments (Clarke and Zaidel, 1989; Marzi *et al.*, 1991). In addition, in our small group of patients, two had a complete commissurotomy, whereas one had a partial commissurotomy sparing the splenium and the tip of the rostrum of the corpus callosum (*see above*). For these reasons, we believe it is important to analyse each subject separately. However, the rationale of the present experiment is to contrast normal subjects with an intact corpus callosum and commissurotomed subjects without one. Thus, we also performed a group analysis of split brain patients. The two analyses are generally consistent with each other.

Individual analysis

D.W. Data are summarized in Fig. 3. Interhemispheric transmission time was 4.05 ms in the basic task, 9.4 ms in the motor task, and 4.5 ms in the visual task. A 3 (task: basic, motor, visual) by 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA revealed no main effect of visual field, a main effect of response hand, $F(1,1390) = 17.3$, $P < 0.001$, with the Lh (274.2 ms) faster than the Rh (283.2 ms), and a main effect of task, $F(1,1390) = 8.9$, $P < 0.001$, with the basic task (278.2 ms) and the motor task (273.4 ms) significantly faster than the visual task (284.6 ms).

The overall response hand by visual field interaction was

significant, $F(1,1390) = 7.5$, $P < 0.007$, whereas all the other interactions were not statistically significant. In particular, there was no task by response hand by visual field interaction. Subsequently, we performed a 3 (task: basic, motor, visual) by 2 (condition: crossed, uncrossed) ANOVA, showing a main effect of task (*see above*), a main effect of condition, $F(1,1396) = 7.3$, $P < 0.007$ (crossed = 281.7; uncrossed = 275.8 ms), but no task by condition interaction.

L.B. Data are summarized in Fig. 4. Interhemispheric transmission time was 27.3 ms in the basic task, 28.45 ms in the motor task and 25.1 ms in the visual task. A 3 (task: basic, motor, visual) by 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA revealed a main effect of visual field, $F(1,1363) = 35.7$, $P < 0.001$, with an advantage of the RVF (301.6 ms) over the LVF (318.6 ms), a main effect of response hand, $F(1,1363) = 105.2$, $P < 0.001$, with the Rh (295.7 ms) faster than the Lh (324.5 ms), and a main effect of task, $F(1,1363) = 33.7$, $P < 0.001$, with the basic task (299.5 ms) and the motor task (305.3 ms) significantly faster than the visual task (325.8 ms).

The overall response hand by visual field interaction was significant, $F(1,1363) = 94.9$, $P < 0.001$, whereas all the other interactions were not statistically significant. In particular, there was no task by response hand by visual field interaction. Subsequently, we performed a 3 (task: basic, motor, visual) by 2 (condition: crossed, uncrossed) ANOVA, showing a main effect of task (*see above*), a main effect of condition, $F(1,1369) = 85.3$, $P < 0.001$ (crossed = 323.8; uncrossed = 297.0 ms), but no task by condition interaction.

N.G. Data are summarized in Fig. 5. Interhemispheric transmission time was 40.6 ms in the basic task, 50.9 ms in the motor task, and 75.9 ms in the visual task. A 3 (task: basic, motor, visual) by 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA revealed a main effect of visual field, $F(1,1363) = 27.5$, $P < 0.001$, with an advantage of the RVF (452.2 ms) over the LVF (489.2 ms), no effect of response hand, and a main effect of task, $F(1,1363) = 72.9$, $P < 0.001$, with the visual task (415.2 ms) significantly faster than the basic task (488.0 ms), which in turn was significantly faster than the motor task (512.6 ms).

The overall response hand by visual field interaction was significant, $F(1,1363) = 66.4$, $P < 0.001$. The task by visual field interaction was also significant, $F(1,1363) = 6.5$,

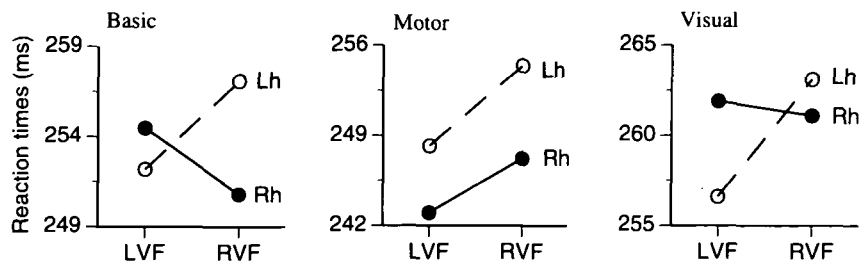


Fig. 2 Visual field by response hand interactions in normal subjects.

of the four visual field–response hand combinations in each subject as the dependent variable, with task as a between-subjects variable, response hand and visual field, or crossed–uncrossed condition as within subjects variables (since a preliminary analysis did not show any difference between index and middle finger in motor task, these constraints were relaxed). Reaction times shorter than 150 ms were considered anticipatory errors, whereas reaction times longer than 500 ms were considered attentional errors and both were removed from the analyses. Interhemispheric transmission time was calculated by subtracting the overall mean for medians of reaction times of the two visual field–response hand combinations subserved by the same hemisphere (uncrossed conditions) from the overall mean for medians of reaction times of the two visual field–response hand combinations requiring an interhemispheric transfer (crossed conditions), and by dividing this difference by two.

Split brain patient's data were analysed individually and as a group. For individual analysis each patient's performance was submitted to ANOVA with trials as the random variable, and task, response hand and visual field, or crossed–uncrossed condition as between-trials variables. For group analysis patients' performances were submitted to ANOVA with trials as the random variable, and patient, task, response hand and visual field or crossed–uncrossed condition as between-trials variables. In all patients, latencies below 150 ms were considered anticipatory errors and they were removed from the analysis. In two patients, L.B. and D.W., reaction times longer than 500 ms were considered attentional errors and they were removed from the analysis. The third patient, N.G., showed long latencies, with an average of >400 ms. In her case, we decided to consider as attentional errors reaction times >3 SDs from their respective condition mean and we removed them from the analysis. Since her performance was generally slower than the other two patients, the group analysis was made with and without N.G.'s data. The two analyses did not show any difference in terms of main effects and interactions. We present here the analysis with all split brain patients' data. Interhemispheric transmission time was calculated by subtracting the overall mean of reaction times of the two visual field–response hand combinations controlled by the same hemisphere (uncrossed conditions) from the overall mean of reaction times of the two visual field–response hand combinations requiring an interhemispheric

transfer (crossed conditions), and by dividing this difference by two. All *post hoc* comparisons incorporated the Bonferroni–Dunn correction for all means.

Results

Normal subjects

Figure 2 summarizes data from normal subjects. Interhemispheric transmission time was 4.3 ms in the basic task, 1 ms in the motor task and 3.65 ms in the visual task. A 3 (task: basic, motor, visual) by 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA revealed no main effect of task, no main effect of response hand, and a main effect of visual field, $F(1,72) = 20.5$, $P < 0.001$, with LVF stimuli (252.8 ms) processed faster than RVF stimuli (255.6 ms).

The overall response hand by visual field interaction was significant, $F(1,72) = 53.8$, $P < 0.001$, whereas the task by response hand interaction fell short of significance, $F(2,72) = 2.757$, $P = 0.06$. Finally, the task by visual field interaction, $F(2,72) = 4.4$, $P < 0.02$, and the task by response hand by visual field interaction, $F(2,72) = 6.3$, $P < 0.004$, were significant.

To further explore these interactions we performed a 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA in each task. There were no main effects of response hand in the basic task and visual task, but there was a main effect of response hand in the motor task (Rh = 245.1 ms; Lh = 251.3 ms), $F(1,24) = 6.5$, $P < 0.02$. There was also no main effect of visual field in the basic task, and there were main effects of visual field in both the motor task (LVF = 245.6 ms; RVF = 250.8 ms), $F(1,24) = 18.1$, $P < 0.001$, and the visual task (LVF = 259.2 ms; RVF = 262.1 ms), $F(1,24) = 8.4$, $P < 0.01$. Finally, there was no significant response hand by visual field interaction in the motor task, but there was a significant response hand by visual field interaction in the two other tasks, basic, $F(1,24) = 32.4$, $P < 0.001$, and visual, $F(1,24) = 24.9$, $P < 0.001$. The absence of the typical response hand by visual field interaction in the motor task was due to a fast crossed LVF–Rh condition (243.0 ms), which was faster than the uncrossed LVF–Lh condition (248.2 ms), $P < 0.001$, and also faster than the uncrossed RVF–Rh condition (247.2 ms), $P < 0.001$.

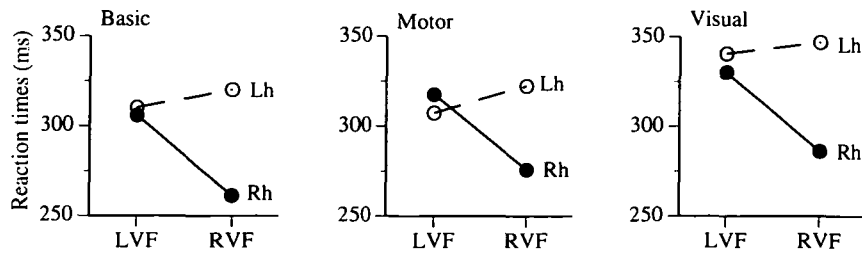


Fig. 4 Visual field by response hand interactions in L.B.

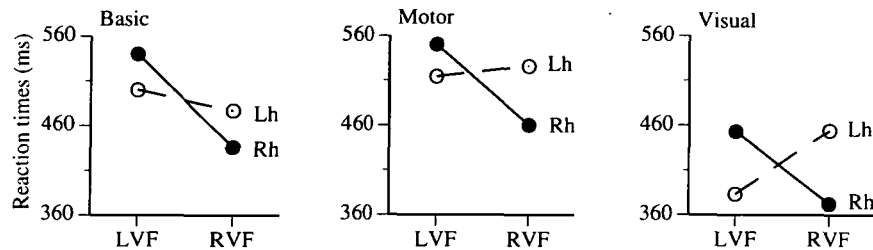


Fig. 5 Visual field by response hand interactions in N.G.

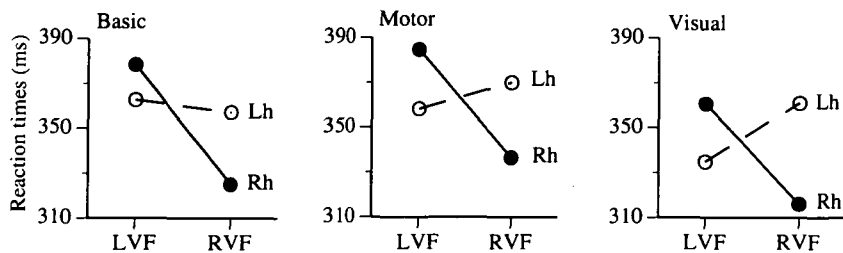


Fig. 6 Visual field by response hand interactions in split brain patients as a group.

$P < 0.002$, due to a significant RVF advantage in the basic task (RVF = 456.0 ms; LVF = 520.4 ms) and in the motor task (RVF = 491.4 ms; LVF = 533.2 ms), but no visual field differences in visual task (RVF = 412.6 ms; LVF = 417.8 ms). None of the other interactions were statistically significant. In particular, there was no task by response hand by visual field interaction. Subsequently, we performed a 3 (task: basic, motor, visual) by 2 (condition: crossed, uncrossed) ANOVA, showing a main effect of task (see above), a main effect of condition, $F(1,1369) = 66.9$, $P < 0.001$ (uncrossed = 442.2; crossed = 499.5 ms), but no task by condition interaction.

Group analysis

Split brain data are summarized in Fig. 6. Interhemispheric transmission time was 24.15 ms in the basic task, 29.65 ms in the motor task and 35.25 ms in the visual task. A 3 (patient: D.W., L.B., N.G.) by 3 (task: basic, motor, visual) by 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA revealed that the overall reaction times of the three patients were different, $F(1,4116) > 200$, $P < 0.001$, D.W. (278.8 ms) being faster than L.B. (310.1 ms), which in turn

was faster than N.G. (470.7 ms). ANOVA revealed also a main effect of response hand, $F(1,4116) = 11.8$, $P < 0.001$, with the Rh (349.2 ms) faster than the Lh (356.3 ms), a visual field effect, $F(1,4116) = 52.3$, $P < 0.001$, with reaction times to RVF flashes (343.0 ms) faster than latencies to LVF flashes (362.5 ms), and a main effect of task, $F(1,4116) = 24.8$, $P < 0.001$, with the visual task (342.3 ms) faster than the motor task (361.1 ms) and than the basic task (354.9 ms). The last two tasks were not significantly different.

The ANOVA also showed an overall response hand by visual field interaction, $F(1,4116) = 134.2$, $P < 0.001$, and a task by visual field interaction, $F(1,4116) = 5.6$, $P < 0.005$. To explore this interaction we performed a 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA in each task, and it revealed a main effect of visual field in the basic task (RVF = 340.4 ms; LVF = 369.6 ms; $P < 0.001$) and in the motor task (RVF = 351.6 ms; LVF = 370.7 ms; $P < 0.001$) but no main effect of visual field in the visual task (RVF = 337.5 ms; LVF = 347.3 ms; NS).

As expected from the individual analysis, the ANOVA also revealed a visual field by patient interaction, $F(1,4116) = 14.1$, $P < 0.001$ (no visual field differences in D.W. and RVF advantage in L.B. and N.G.), a response hand by patient

interaction, $F(1,4116) = 18.1$, $P < 0.001$, (Lh advantage in D.W., Rh advantage in L.B. and no difference in N.G.), a task by patient interaction, $F(1,4116) = 82.0$, $P < 0.001$, (the fastest tasks in D.W. and L.B. were basic and motor, whereas in N.G. the fastest task was visual), and a patient by response hand by visual field interaction, $F(1,4116) = 32.1$, $P < 0.001$ (due to the large difference in interhemispheric transmission time between the patients).

Finally, the analysis of split brain data showed that the task by response hand interaction, which approached significance in normal subjects, and the task by response hand by visual field interaction, which was significant in normal subjects, were no longer significant in commissurotomed patients. A 2 (response hand: Rh, Lh) by 2 (visual field: RVF, LVF) ANOVA in each task revealed no main effect of response hand in all tasks, and a response hand by visual field interaction in all tasks ($P < 0.001$ for all interactions). The four-way interaction patient by task by response hand by visual field was also not significant. Subsequently, we performed a 3 (patient: D.W., L.B., N.G.) by 3 (task: basic, motor, visual) by 2 (condition: crossed, uncrossed) ANOVA, showing a main effect of task (*see above*), a main effect of patient (*see above*), a main effect of condition, $F(1,4134) = 132.0$, $P < 0.001$ (uncrossed = 337.9; crossed = 367.8 ms), a patient by condition interaction, $F(1,4134) = 32.2$, $P < 0.001$ (due to the large difference in interhemispheric transmission time between patients), but no task by condition interaction and no patient by task by condition interaction.

Discussion

The rationale of the present study arises from the possibility of simultaneous asymmetries in callosal relay, stimulus processing and motor response in the Poffenberger's paradigm. We contrast the effect of two manipulations of the paradigm on the behaviour of different populations, normal subjects and split brain patients, in order to test the relative contribution of each component to the asymmetric visual field by response hand pattern showed by the meta-analysis (Marzi *et al.*, 1991). We reasoned that an increase in visual field difference during the visual task and an increase in response hand difference during the motor task, without any change in interhemispheric transmission time, in both normals and split brain patients, would indicate a hemispheric contribution. On the other hand, if the experimental manipulations affect the interhemispheric transmission time (indexed by a three-way interaction of task by response hand by visual field and a two-way interaction of task by crossed–uncrossed condition) in normal subjects but not in commissurotomed patients, then this would indicate changes in callosal relay due to the experimental manipulations. In addition, if the fastest pathways control behaviour, as suggested in the model of transmission time by Clarke and Zaidel (1989), only the manipulation affecting the fastest (motor) channel should be effective in changing

significantly the transmission time, since the effect of the manipulation affecting the slow (visual) channel should be 'masked' by the faster transmission time of the fast channel.

Data from normal subjects show that the motor task enhanced response hand differences (significant advantage for the Rh in the motor task, no difference between hands in the basic task), and that the visual task enhanced visual field differences (LVF advantage in the visual task and no difference in the basic task). Moreover, the three-way interaction of task by response hand by visual field and the two-way interaction of task by crossed–uncrossed difference were significant, with the response hand by visual field interaction and the difference between crossed and uncrossed conditions, typically observed in this task, being significant in the basic task and the visual task but not in the motor task (Fig. 2). Indeed, a surprising advantage for the crossed LVF–Rh condition over the uncrossed LVF–Lh and RVF–Rh conditions was observed during the motor task.

Split brain patients, both individually and as a group, do not show a response hand by task interaction. However, the visual task enhanced LVF performance in split brain patients as a group and in N.G. individually. Although his individual visual field by task interaction was not statistically significant, D.W. also shows a relative improvement of LVF performance compared with RVF performance from the basic to the visual task. The group analysis shows that the RVF advantage observed in the basic task and in the motor task, which is consistent with previous findings in split brain patients (Sergent and Myers, 1985; Clarke and Zaidel, 1989; Marzi *et al.*, 1991) and may be related to some technical aspects of the surgical procedure that are more likely to produce a small extra-callosal damage in the right hemisphere rather than in the left hemisphere (Bogen, 1993), is no longer present in the visual task, and this is not due to a slowing down of the RVF (the overall reaction times for RVF stimuli in visual task is even faster than the other two conditions) but to a speeding up of the LVF (~23 ms from the basic task and the motor task to the visual task).

The most striking difference between normals and split brain patients appears to be the lack of the three-way interaction of task by response hand by visual field and the lack of the two-way interaction of task by crossed–uncrossed difference in commissurotomed subjects. Thus, taken together, both manipulations meet the criteria we outlined in our rationale. The motor task enhanced the differences between response hands but it also affected significantly the response hand by visual field interaction and the crossed–uncrossed difference in normal subjects, but not in commissurotomed patients. The visual task enhanced LVF performance (relative to RVF) in both groups and it did not affect the visual field by response hand interaction or the crossed–uncrossed difference. In other words, according to our predictions, the visual condition affected only the hemispheric contribution to the behavioural pattern, whereas the motor condition also affected the callosal relay contribution, probably producing a change in the channel

responsible for the interhemispheric transfer. Moreover, the parallel behaviour in the motor and the visual task observed in the complete and partial split brain patients confirms that the visual channel is not responsible for the observed change in callosal relay in normals. Otherwise, we should have observed the same change in the partial commissurotomy patient with the spared splenium of the corpus callosum. Note that in spite of striking differences in overall reaction times, interhemispheric transmission time, main effect of response hand and of visual field, the patients consistently failed to show significant task by response hand by visual field and task by crossed–uncrossed interaction, and responded to the two different new versions of the task in the same way.

The observed advantage of the crossed LVF–Rh condition over the two uncrossed conditions in the motor task is surprising and requires some speculation. It can be interpreted as a facilitation of interhemispheric connections or as an inhibition of intrahemispheric connections or both. Since the presence of an intact corpus callosum seems to be necessary for this effect (it was observed in normal subjects but not in split brain patients), we think that the hypothesis of an inhibition of intrahemispheric connections alone is unlikely. We believe that the observed changes can be accounted for at three different callosal levels: at the level of motor–motor connections, at the level of premotor and supplementary motor area connections, and at the level of associative visuomotor connections.

Regarding the motor–motor connections, recent studies have demonstrated shortened simple reaction times with focal transcranial magnetic stimulation delivered over the motor cortex ipsilateral to the responding hand, suggesting that transcallosal connections may disinhibit or activate the excitability of the contralateral motor cortex (Pascual-Leone *et al.*, 1992a, b). A neuroanatomical study has also provided evidence for interhemispheric connections of the motor cortices even for distal muscles of the hand (Gould *et al.*, 1986), so that transcallosal facilitatory mechanism may be involved in the shortening of LVF–Rh reported in the present study. Our experiment showed that if this mechanism was effective, then it was confined to the right hand. Unfortunately, in the neurophysiological studies cited above (Pascual-Leone *et al.*, 1992a, b) the motor response was confined to the right arm, and we do not know if the same facilitating effects can be elicited in the opposite arm. However, calling for such an asymmetric mechanism seems to us an unparsimonious explanation.

Regarding premotor and supplementary motor area connections, in our motor task the subjects were requested to alternate index and middle finger for odd and even trials. The requested motor response was unambiguously described, as simple reaction times tasks require (Luce, 1986). Nonetheless, it requires the subjects not only to prepare the response of the correct finger in the current trial, but also to inhibit the motor response of the inappropriate finger. We designed this task assuming that premotor areas and the supplementary motor area must be involved in planning such

a motor response (Goldberg, 1985). Evidence for a dominant role of the right supplementary motor area in such a task has in fact been reported in brain-damaged patients (Verfaellie and Heilman, 1987). However, it is not immediately clear how such a proposed dominance can be translated into a facilitatory effect in the Rh only when the visual stimulus is confined to the right hemisphere.

Neither the motor–motor connections nor the premotor and/or supplementary motor area connections hypothesis can account for the large LVF advantage observed in the motor task in normal subjects. This effect was not predicted and it is even larger than the predicted LVF advantage in the visual task (5.2 ms advantage for the LVF in the motor task and 2.9 ms advantage for the LVF in the visual task). The absence of a corresponding increase in LVF performance in the motor task in split brain patients (the same patients showed an increase in LVF performance in the visual task, parallel to the increase showed by normal subjects) suggests that the large LVF advantage observed in normals in the motor task is related to the presence of the corpus callosum and of intact visuomotor interhemispheric connections. Models of sensorimotor transformations in the human brain invoke diverse mechanisms, such as efference copies of motor commands (Andersen *et al.*, 1987), attentional mechanisms directed by the posterior parietal cortex (Andersen, 1987), or even a direct command apparatus in posterior parietal cortex (Mountcastle *et al.*, 1975). Posterior parietal cortex is extensively interconnected with other regions of the brain, both ipsilateral and contralateral, among them premotor areas and supplementary motor area (Cavada and Goldman-Rakic, 1989b). The interhemispheric connections include both homotopic and heterotopic areas which largely duplicate the ipsilateral connections (Cavada and Goldman-Rakic, 1989a). This widespread distribution of heterotopic contralateral connections plus some features exhibited by heterotopic callosal pathways in general, which are typical of association projections, have been interpreted as suggestive of an integrative role (Kennedy *et al.*, 1991; Stein, 1992). We propose that the attentional demand of alternating a motor response during the motor task transformed the task to a resource-limited one, making it necessary to re-allocate resources, relative to the basic task. On this account, the re-allocation of resources would have been subserved by the interhemispheric visuomotor heterotopic connections and would have favored a fast right-to-left transmission of information rather than a fast left-to-right or even intrahemispheric transmission of information. However, this proposal remains hypothetical and must be substantiated by further studies.

A final comment regards the manipulation of the eccentricity of the visual stimulus that is part of the visual task. The manipulation of eccentricity with respect to the vertical meridian is known to affect overall reaction times in normal subjects and to affect both reaction times and interhemispheric transmission time in commissurotomy patients. In our visual task the visual stimuli were presented

both at 4° of eccentricity from the vertical meridian (as in the basic task) and at larger eccentricities. Therefore, on average, the eccentricity of the visual task was larger than the eccentricity of the basic task. Indeed, in normals, the visual task was the slowest one, albeit not significantly. The slowing down was not significant, probably due to the between-subjects design that we adopted. We used this design since Poffenberger's paradigm demands a large number of trials to reduce the 'noise', and our three different tasks would have led to a very large number of trials per subject, i.e. more than 1600! The same effect applies to interhemispheric transmission time in the split brain patients. In the visual task the transmission time, though not significantly different from the transmission time of the other two conditions, is certainly the slowest one. The significantly faster overall reaction times observed in the visual task in the group analysis of split brain patients, on the other hand, may be due to peculiarities in the orienting of attention in these patients (Zaidel, 1994).

In conclusion, the results of the present study support the notion that the corpus callosum is composed of several different channels, each having its own properties and transmission time, and that these channels can modulate interhemispheric communications in a dynamic fashion. Nonetheless, the complex relationships between the different callosal channels are still largely unexplored and deserve further investigation.

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