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"Callosal Pathways for Simple Visuomotor Control in Man"

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8.5 Callosal Pathways for Simple Visuomotor Control in Man

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8.5.1 Simple Visuomotor Control

In ordinary life conditions, many human movements occur under visual control and therefore require a functional coordination between visual and motor centers in the cerebral cortex as well as in subcortical centers. Complex sequences of activation of visual and motor centers have been postulated to underlie those motor responses which must be shaped and/or continuously guided by the visual stimulus as actually perceived or remembered (e.g., Glickstein 1990). In more elementary forms of visuomotor integration visual stimuli may act merely as triggers for simple motor responses which, once initiated, can proceed unaided by visual perception or memory. At least the fastest of these responses can be emitted in a reflexlike fashion, such that the underlying neural circuits are likely to involve relatively fixed and straightforward connections between visual and motor cortical areas.

In 1912 Poffenberger applied chronometric analysis to the dissection of the central neural pathways subserving the execution of a fast manual or digital movement (such as pressing a key) in reaction to a light flash presented in the right or left hemifield, that is, to the visual cortex of the opposite hemisphere. The motor reaction of each hand is under the control of the contralateral hemisphere due to the crossing of the major motor pathways.

Uncrossed reactions (i.e., reactions of each hand to stimuli in the ipsilateral hemifield) can thus be integrated within a hemisphere, whereas crossed reactions (i.e., reactions of each hand to contralateral hemifield stimuli) require an interaction between the hemisphere receiving the visual stimulus and that emitting the response, probably through the corpus callosum. On this basis Poffenberger (1912) argued that the reaction time (RT) of crossed responses should be longer than that of uncrossed responses, and that the crossed-uncrossed time difference (CUD) should correspond to the additional time needed for interhemispheric communication. He found a CUD of a few milliseconds in the expected direction, and his finding has been repeatedly confirmed by modern studies which have demonstrated CUDs of 2–3 ms, a difference which can be accounted for by the conduction time along the largest fibers of the corpus callosum (Bashore 1981: Aglioti et al. 1993: Tassinari et al. 1993).

8.5.2 Crossed Visuomotor Control in Patients with Partial or Complete Callosal Defects

If the corpus callosum is crucially involved in the fast integration of crossed responses, the execution of these responses should be impossible or very slow in acallosal subjects. To test these possibilities we measured the CUD in six subjects with an callosal section sparing the splenium, one subject with total section of the corpus callosum, two subjects with complete callosal agenesis, and one subject with an agenetic absence of the splenium due to a cerebrovascular malformation. The callosotomy patients had been suffering for several years from drug-resistant forms of epilepsy and had been submitted to section of 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) showed the completeness of the callosal section in one case whereas in the remaining cases the extent of the callosal section varied from the anterior one-third to the anterior four-fifths of the corpus callosum, the splenium being consistently spared. In the three subjects with dysgenetic callosal defects MRI showed a complete absence of the corpus callosum in two cases, whereas in the third only the posterior third of the callosum with the splenium was lacking, most probably because its development was prevented by an arterovenous malformation attached to the great cerebral vein of Galen. The rest of the corpus callosum is normal in the latter patient. Detailed descriptions of these cases can be found in Aglioti et al. (1993) and Tassinari et al. (1993).

Table 1 shows that CUDs of the subjects with partial callosal defects, whether surgical or congenital, fell by and large within the normal range. By

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Normal subjects ($n=12$) (Di Stefano et al. 1980)	2.2 ± 0.4
Normal subjects ($n=8$) (Tassinari et al. 1983)	2.7 ± 1.3
Normal subjects ($n=48$) (Aglioti et al. 1991)	7.4 ± 1.9
Anterior callosotomy patients ($n=6$) (Tassinari et al. 1993)	3.3 ± 2.8
Complete callosotomy patient ME (Aglioti et al. 1993; Tassinari et al. 1993)	83.2
Complete callosal agenesis patient RB (Aglioti et al. 1993; Tassinari et al. 1993)	22.5
Complete callosal agenesis patient PM (Aglioti et al. 1993; Tassinari et al. 1993)	25.4
Posterior callosal agenesis patient AZ (Tassinari et al. 1993)	11.8

Table 8.5–1. Crossed-uncrossed differences in reaction time (ms) Data for groups are means ± standard errors of the mean. Note the abnormally prolonged CUDs of patients with complete callosal defects (ME, RB, PM). The CUD of patient AZ with a posterior callosal defect, although slower than the normal mean CUDs, is still within the normal range.

contrast, the CUDs exhibited by the two subjects with a complete callosal agenesis and by the subject with a complete callosal section were at least an order of magnitude greater than the typical 2–3 ms CUDs of normals. These findings confirm previous reports of abnormally prolonged CUDs values in subjects with a congenital absence of the corpus callosum (e.g., Milner et al. 1985; Di Stefano et al. 1992) as well as in split-brain patients (Sergent and Myers 1985; Clarke and Zaidel 1989; Di Stefano et al. 1992). In addition, the contrast between the presence of an abnormal prolongation of CUDs in the completely acallosal subjects and its absence in the subjects with partial callosal defects, whether anterior or posterior, suggests that both anterior and posterior callosal routes can subserve the integration of speeded crossed responses.

8.5.3 Callosal and Non-Callosal Mechanisms of Crossed Visuomotor Control

In principle, 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 (Berlucchi 1978). The fact that CUD remains 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 (Berlucchi 1978; Milner and Lines 1982; Milner et al. 1985). 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 (Rugg et al. 1984). 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. Some 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 (De Lacoste et al. 1985). 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 (Andersen 1987), and very long CUDs have been reported in patients with parietal lesions (Anzola and Vignolo 1992). Conceivably, parietal regions with callosal connections running in the splenium may have a role in coordinating motor initiation functions across the hemispheres (Tassinari et al. 1993).

More direct evidence for the normal involvement of the corpus callosum in the fast integration of crossed manual responses has been obtained by studying CUDs for responses to unilateral flashes performed bilaterally and/or with effectors other than the hands. Studies in normals (Di Stefano et al. 1980) have borne out a clearcut distinction between crossed responses which presumably utilize interhemispheric transfer from those which presumably do not. The first set of responses includes unilateral and bilateral distal responses (e.g., flexion of the thumb) and unilateral proximal responses of the upper limb (e.g., flexion of the elbow), all associated with significant CUDs reflecting dependence on interhemispheric transfer. The second set includes bilateral proximal responses and unilateral and bilateral axial responses of the upper limb (e.g., elevation of the shoulder), all associated with null CUDs reflecting independence from interhemispheric transfer. Logically this distinction leads one to predict that impairment of interhemispheric transfer by callosal defects should alter the CUDs associated with the first set of responses, but not those associated with the second set. The CUD pattern that we found in our three subjects with complete callosal defects, either surgical or dysgenetic, fitted this prediction very well (Aglioti et al. 1993). As with normal subjects, these acallosal subjects showed insignificant CUDs for bilateral proximal responses and for unilateral and bilateral axial responses, in sharp contrast with their greatly prolonged CUDs for distal responses, either unilateral or bilateral, and for unilateral proximal responses. These results confirm that a callosal contribution is important for the execution of fast distal and uni-

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lateral proximal responses to a visual stimulus directed to the hemisphere ipsilateral to the responding hand. The importance of the corpus callosum derives from the fact that motor pathways for manual or digital movements are completely crossed. By contrast, other upper limb movements can be directly initiated by either hemisphere through bilaterally distributed motor pathways. Bilaterally distributed motor systems originating from each hemisphere are indeed available for the activation of axial and proximal limb muscles involved in global body movements, general postural adjustments, and integrated synergistic limb-body movements. Their existence has been demonstrated anatomically and physiologically in nonhuman primates (Kuypers 1987; 1989) and confirmed by clinical and experimental evidence in man (e.g., Freund 1987; Colebatch and Gandevia 1989; Müller et al. 1991; Colebatch et al. 1991; Benecke et al. 1991). Thus it is possible for a visual input channeled into a single hemisphere to directly initiate and guide axial and proximal limb movements on both sides of the body, and this is why CUDs are absent in normal and acallosal subjects when crossed as well as uncrossed visuomotor responses can be initiated by the hemisphere receiving the flash without the aid of the corpus callosum.

It must be emphasized that our completely acallosal subjects were fully capable of making all types of speeded responses both ipsilaterally and contralaterally to the visual stimulus on both right and left sides. Their strikingly long CUDs depended on a selective retardation of crossed responses relative to uncrossed responses. Crossed responses appear to be mediated in these subjects by an extracallosal interhemispheric transfer via relatively long cross-midline pathways which are able to transmit at least crude visual information. Several considerations suggest that this transfer occurs by way of subcortical commissures and other brainstem routes for indirect communication between the cortices of the two sides (Aglioti et al. 1993), as has been postulated to account for residual abilities for interhemispheric interaction in visually guided behavior in callosal agenesis and after forebrain commissurotomy (Trevarthen and Sperry 1973; Holtzmann 1984; Milner 1982; Milner et al. 1985; Myers and Sperry 1985; Sergent 1986, 1987).

8.5.4 Extracallosal Interhemispheric Transfer of Simple Visual Information

We obtained internal additional evidence for an abnormally slow interhemispheric transmission of crude visual information in our subject with a complete callosotomy. We used a two-flash paradigm in which subjects must detect a first extrafoveal flash of light (or prime) without overtly reacting to it, and then press a key as fast as possible upon seeing a second extrafoveal

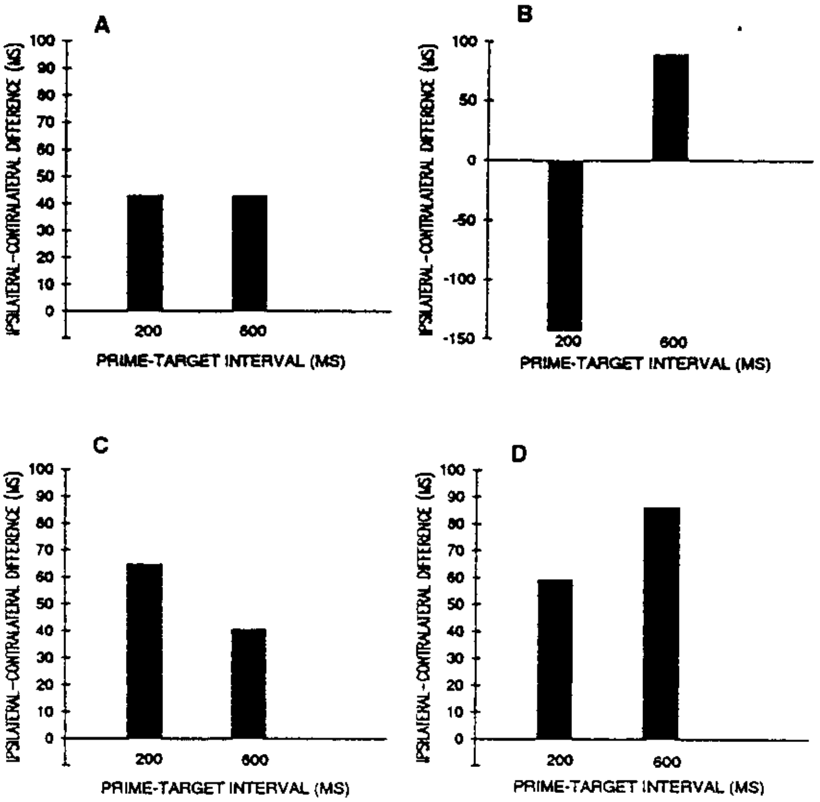

Fig. 8.5–1. Differences between RT for ipsilateral prime-target combinations and RT for contralateral prime-target combinations as a function of prime-target interval in 6 normal subjects (A,C; from Tassinari et al. 1987) and in the completely callosotomized patient ME (B,D). The stimulus array was aligned with the horizontal meridian in A,B and with the vertical meridian in C,D

flash (target). During the presentation of both prime and target as well as in the prime-target interval the eyes must remain fixated on a mark in front of the subject. Normal subjects are faster in reacting to targets contralateral than to targets ipsilateral to the prime (Fig. 1A). When prime and target are presented in the same visual hemifield they can be processed by the same hemisphere, whereas with contralateral combinations the prime and the target are processed by different hemispheres, and therefore an interhemispheric integration is required for the execution of the task. Nevertheless, the response speed for ipsilateral prime-target combinations is subject to an inhibition which annuls and overrides the advantage of intra-over interhemispheric integration (Posner and Cohen 1984; Tassinari et al. 1987; Berlucchi et al. 1989). But if the interhemispheric exchange of visual information subserving the response to contralateral prime-target combinations is slowed down by the absence of the corpus callosum, then one might expect RT for contralateral combinations to be longer than RT for ipsilateral combinations, in spite of ipsilateral inhibition. As shown in Fig. 1B, this is precisely what we found in our completely callosotomized subject. In support of the hypothesis of a slow interhemispheric transmission of visual information via an extracallosal route in this subject, the relative contralateral advantage was absent at short but present at long intervals between prime and target. At short intervals, the impairment of interhemispheric communication overrode ipsilateral inhibition. By contrast, ipsilateral inhibition was evident in normals at both short and long intervals because of the rapid interhemispheric transmission. Ipsilateral inhibition can also be demonstrated in normal subjects with primes and targets presented along the vertical meridian (Fig. 1C). In this case ipsilateral inhibition occurs with combinations involving primes and targets occurring on the same side of (i.e., both below or both above) the horizontal meridian (Berlucchi et al. 1989). However, primes and targets are projected to both hemispheres with both ipsilateral and contralateral combinations, and therefore the latter combinations do not require interhemispheric cooperation. Accordingly, Fig. 1D shows a completely normal ipsilateral inhibition in the completely callosotomized subject tested with primes and targets presented along the vertical meridian. This result provides further evidence for a causal role of the callosal disconnection in the abnormal response to horizontal stimuli at short prime-target intervals.

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