Ital. J. Neurol. Sci. 13:649-655, 1992

Interhemispheric communication following unilateral cerebrovascular lesions

Anzola G.P., Vignolo L.A.
Clinica Neurologica dell'Università, Brescia

39 patients with a single small cerebrovascular lesion (20 in the right, 19 in the left hemisphere) were subjected to a simple reaction time (RT) task with visual stimuli flashed to the visual field either ipsilateral or contralateral to the cerebral lesion. The subject responded always with the ipsilateral hand. The crossed-uncrossed difference (CUD), i.e. the RT when both stimulus and response occur on the same side minus the RT when stimulus and response occur on opposite sides, is assumed to assess the transit time of information through callosal fibers, and in normal people is about 3-5 msec. In our patients the mean CUD, expressed as the difference between contralateral and ipsilateral responses, was 20 msec. Patients with parietal lesions had still longer CUDs, 37 msec on the average. There was no statistical difference in CUDs between right and left brain-damaged patients.
The CUD in brain-damaged patients was of the same order of magnitude as that found in acallosal or split-brain patients. Nonetheless, the present findings are interpreted as reflecting the intrahemispheric rather than the interhemispheric delay in information transmission, with the possible additive effect of an asymmetrical orienting of attention.

Key Words: Interhemispheric communication — reaction time — cerebrovascular diseases.

Introduction

Manual Reaction Time (RT) to lateralized visual stimuli can be used to assess callosal transfer time. If the stimulus is delivered, e.g., to the right visual field (RVF), projecting to the left hemisphere, and the subject has to respond with the right hand (RHd), also controlled by the left hemisphere, all the operations involved in the task may be performed within the same hemisphere, in this case the left (See figure 1b). On the other hand, when the stimulus is flashed in the left visual field (LVF), the processing of the stimulus occurs in the right hemisphere, but the initiation of the response is operated by the left hemisphere. In this condition the information must cross the interhemispheric commissures to link the "receptor" to the "effector" hemispheres (Fig. 1a).
Assuming that the cognitive operations remain the same, the uncrossed condition (RVF-RHd) is expected to yield RTs faster than the crossed condition (LVF-RHd) by an amount equal to the commissural transit time. Obviously the same reasoning applies to the responses of the left hand when stimuli are presented either to the left or to the right visual field. Therefore, the CUD (crossed-uncrossed difference, i.e. RT in the crossed condition minus RT in the uncrossed condition) re-

Received 28 February 1992 - Accepted 22 June 1992

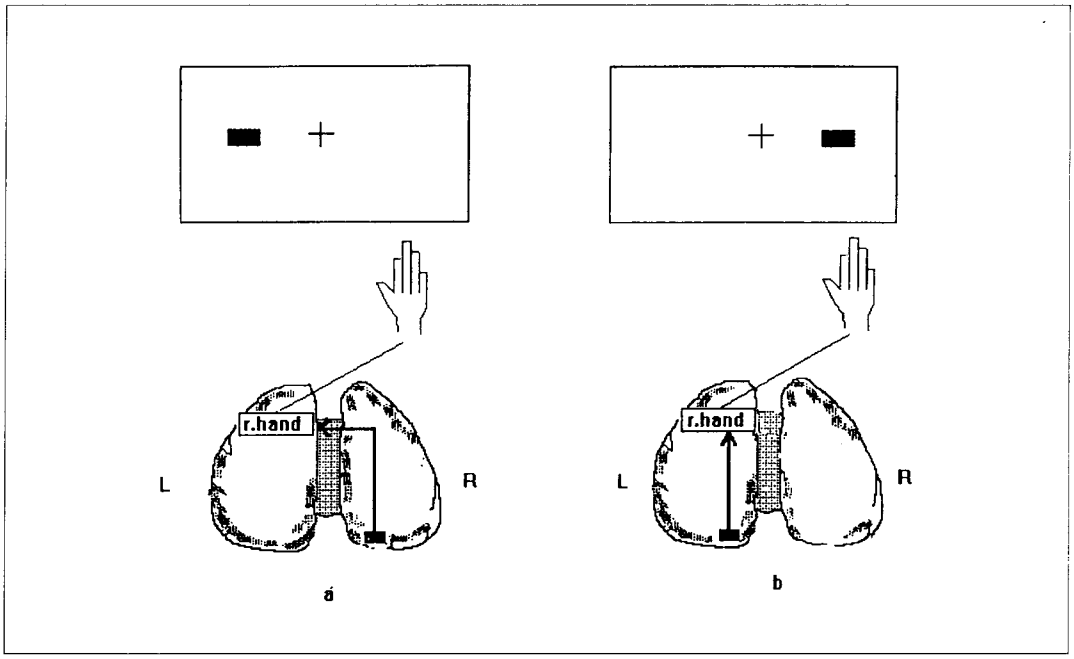

Fig. 1.

presents an estimate of the delay due to callosal transmission, or, in other words, of the callosal transit time.

In normal humans such a delay has been estimated to be in the order of 2-5 msec. [1, 6, 14, 18, 24], which is consistent with the conduction time of the large fibers of the human corpus callosum [25], whereas in subjects congenitally lacking the corpus callosum as well as in patients subjected to surgical section of the forebrain commissures, the CUD is enormously increased, up to 70 msec [10].

Little is known about the effects of unilateral brain lesions on CUD. In a recent paper a difference of 350 msec. was reported between contralateral and ipsilateral RTs in an unselected sample of right brain-damaged patients responding with the hand ipsilateral to the brain lesion [10]. However, it is doubtful whether this difference truly represents interhemispheric delay or the effect of other factors such as attentional shifts or visual field defects.

In the present investigation we have measured the CUD in a carefully selected sample of right and left brain-damaged patients with the aim of clarifying whether: 1) the absolute values are comparable to those of normal people and 2) the side of the cerebral lesion affects interhemispheric transmission.

The data reported here were obtained in a larger study on RTs in brain-damaged patients [2]. Therefore, the procedure is only briefly summarized here. For further details the reader is referred to reference n. 2.

Patients and Methods

The sample consisted of 20 — 15 male and 5 female — right brain-damaged (RBD) and 19 — 13 male and 6 female — left brain-damaged (LBD) patients, all right-handed (19), with single small vascular lesions assessed by CT scan. Mean age and educational level were respectively 50 and 5.9 years in the RBD group vs 56 and 6.6 in the LBD group. The RTs were collected on average 18.5 days after the stroke in RBD and 22 days post stroke in LBD patients. The severity of the hemiparesis, assessed on a semiquantitative scale, was 2.5 and 2.9 in RBD and LBD patients respectively (0 = no movement; 1 = possible spontaneously; 2 = possible against resistance; 3 = possible against gravity; 4 = normal). All the patients were subjected to careful evaluation with Goldman kinetic perimetry and had no visual field defect. Finally, they were free of significant neuropsychological abnormalities as assessed by the Token Test [11], the Benton's Line Orientation test

TABLE I. *Mean and SD (in parentheses) of RTs in milliseconds.*

	Stimulus side	
	Ipsilateral	**Contralateral**
Right Brain damaged	296 (109)	316 (120)
Left Brain damaged	290 (90)	310 (92)

[5] and the Raven Colored PM 1947 [3]. Aphasics among LBD and hemineglect patients among RBD were excluded from the study.

The lesions were mapped onto a lateral diagram of the brain using a computerized version of the procedure described by Mazzocchi and Vignolo [15]. Lesion size was determined as described in [2]. The visual stimulus, a bright dot, was flashed 3 degrees to the right or left of the central fixation point either in blocked (i.e. the stimulus appeared always in the same location) or in random presentations (i.e. the stimulus appeared randomly in the right or left visual field). The patients responded with the hand ipsilateral to the lesion side. Two hundred RTs were collected in each visual field both in the blocked and in the random condition. The order of condition and visual field was balanced across patients. The median of RTs was used for statistical analysis.

Results

The mean scores of neuropsychological tests in RBD patients were: Token Test = 33 ± 2.5, Benton's Line Orientation test = 20.3 ± 5.8, Raven Colored PM = 28.5 ± 5.2. The LBD patients' performance on the same tests scored 29.9 ± 6.7, 20.8 ± 5.7 and 28.3 ± 8.1 respectively. There was no difference on either comparison, although LBD patients had a mean lower score than RBD patients in the Token Test.

Reaction time

The medians of the RTs were entered in a repeated measures ANOVA with lesion *side* as the only between-subjects variable and *condition* (blocked vs random) and visual *field* (ipsilateral vs contralateral) as within-subjects variables. The results are shown in Table I.

No difference was found between right and left brain-damaged patients in the overall speed of response. The blocked condition elicited faster responses than the random condition (295 vs 311 msec.; $p<0.005$ — not shown in table I). The RTs to the stimuli presented ipsilaterally to the lesion were faster than the RTs to the stimuli presented contralaterally (293 vs 313; $p<0.001$). Since the subjects responded always with the hand ipsilateral to the lesion, the ipsilateral RT is the uncrossed response and the contralateral RT is the crossed response. Therefore the difference between contralateral and ipsilateral RTs corresponds to the crossed-uncrossed difference, i.e. the CUD. As is shown in Table I the mean CUD was of $313 - 293 = 20$ milliseconds.

None of the interactions proved significant, although there was a trend for the condition × field interaction ($F = 3.001$, $p = 0.09$). This means that the CUD tended to be smaller in the blocked than in the random condition, the corresponding figures being 15 and 24 msec. respectively. On the other hand, the CUD in right brain-damaged patients was the same as in left brain-damaged patients (20 msec.). Finally the CUD did not depend on the speed of the response, as the correlation coefficient between CUDs and RTs was 0.017.

Lesion characteristics

The mean volume of the lesion was 8.5 (±15.9) ml for RBD patients and 5.2 (±12.5) ml for LBD patients. This difference was not statistically significant ($t = 0.65$, d.f. 31, $p = 0.520$). Further analyses were done on RTs and CUDs in relation to lesion size and site. Simple regression analysis showed that in LBD patients CUDs linearly increased with lesion volume ($F = 18.896$, $p = 0.0008$). However, in RBD patients such a relation was absent. The same negative result was obtained when both groups of patients were analyzed together.

To investigate the impact of lesion site, we first compared cortical to subcortical lesions. No difference emerged from the t test. The next step was to regroup patients according to the extent of damage in each cerebral lobe and to compare CUDs of this group with those of the rest of the sample. Extent of the lesion in the frontal, temporal and/or occipital lobes yielded no significant differences with respect to the rest of the sample. However, when patients were grouped for parietal involvement, a significant difference emerged in CUDs. Out of the total sample of 39 patients, there were 11 patients in whom the lesion extended to the parietal lobe. The mean CUD in these patients was 37 ± 30 msec., whereas the rest of the sample showed a mean CUD of 13 ± 26 msec. ($t = 2.494$, $df = 37$, $p = 0.017$). By contrast the overall RTs and the lesion volumes of parietal patients were not statistically different from RTs and lesion volumes of the remainder of the sample. Finally, left parietal patients were not different from right parietal patients as far as RTs, CUDs

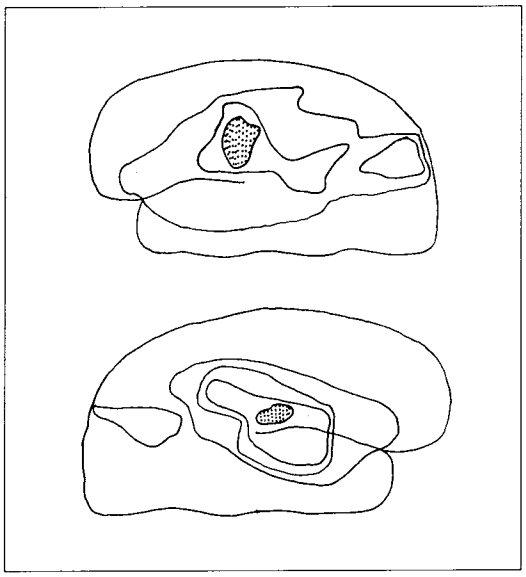

Fig. 2. *Approximate extent of lesioned areas in the left (top) and right (bottom) hemisphere in patients with parietal lesions assessed by CT scan. Contours do not indicate individual lesions but the degree of overlapping lesions in a given area, they represent the boundaries of areas damaged by one lesion only (outer area), by two or by three lesions, etc. Dots cover the areas of maximum overlap. (See (15) for details on the mapping procedure).*

and lesion volume are concerned. The composite contour maps [26] of the lesions of parietal patients are shown in Fig. 2.

Discussion

The assessment of CUD has proved valuable for studying the time of information transfer between the cerebral hemispheres. In the uncrossed condition, the stimulus is delivered to the hemisphere that initiates the response (this condition corresponds to the ipsilateral responses in our experiment). By contrast, in the crossed condition the stimulus is projected to one hemisphere and the response is produced by the hand controlled by the other hemisphere, requiring a passage of information across the forebrain commissures. Note that in our experiment this condition corresponds to the contralateral responses. The CUD may be obtained either with blocked or with random presentations. In normal subjects the CUD is remarkably constant, in the order of 1-3 msec., and invariant whether the stimuli are presented in the blocked or in the random modality [1, 14, 17, 18, 24]. However, the absolute values of RTs rise in the random presentations [14], probably due to the different attentional demands of the two tasks: in the blocked condition the subject knows in advance where the stimulus is going to appear and so he can direct his attention in advance to the presentation side, whereas in the random condition, he can either spread attention over the whole field or guess which field will be stimulated (but in this case there is 50% chance of mistaking the target). Either way, before he can respond he must shift attention to the stimulus. This extra operation, which requires a measurable time to carry out, brings about a delay in the overall RTs, but is not expected to affect the interhemispheric transmission time. The CUD remains the same, despite an increase in RTs from the blocked to the random situation [14].

Our findings in brain-damaged patients showed the expected effect of the modality of presentation on RTs, as blocked RTs were 16 msec. faster than random RTs (295 vs 311 msec respectively), but they also showed CUDs of 20 msec. on the average, far greater than those obtained in normal subjects and comparable to those attained by acallosal patients (see [10] for a review). In brain-damaged patients, too, CUDs tended to increase from the blocked to the random condition (15 vs 24 msec. respectively) although the difference was not statistically significant. Parietal lesions produced CUDs of 37 msec., which were significantly longer than the 15 msec. CUDs of the rest of the sample. In conclusion, then, in unilaterally brain-damaged patients we found both a general retardation in CUDs, irrespective of lesion site, and a further retardation produced by parietal lesions. This result can be interpreted in several ways. The first is that the increased CUDs were produced by a general lengthening in RTs, which is known to occur in brain-damaged patients [4, 17]. We can confidently rule out this explanation, first because when RTs are pathologically slow, relatively minor differences generally tend to be obscured rather than amplified, second and more directly because there was no correlation between RTs and CUDs, and parietal patients, who had the slowest CUDs, did not differ from the rest of the cohort in overall RTs.

Another possibility is that abnormal CUDs were a consequence of visual field defects contralateral to the damaged hemisphere, which could have impaired the detection of the stimulus in the crossed condition. However this seems unlikely, as all patients were subjected to careful evaluation with Goldman kinetic perimetry and had no visual field defect. Moreover, deepseated lesions were as effective as superficial lesions in lengthening the CUDs.

Assuming no impairment at the visual stage of information processing, we must concede that the cerebral lesion somehow affected the transfer of information from the occipital pole of the dam-

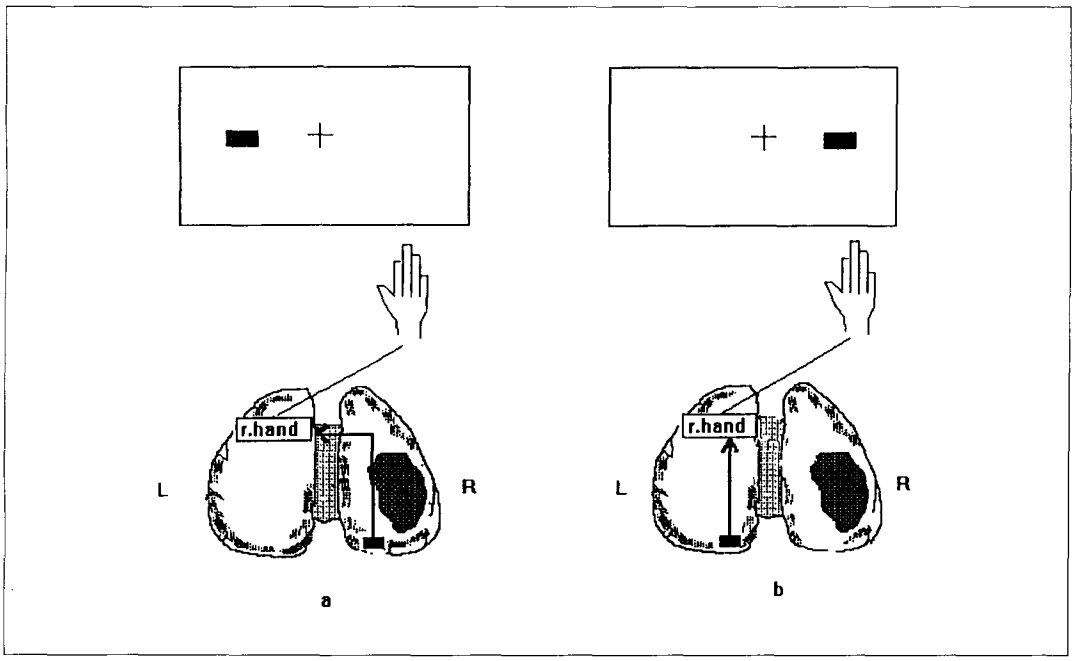

Fig. 3.

aged hemisphere to the motor area of the contralateral one. In normal individuals the CUD is believed to represent the interhemispheric transit time of nonsensory information, since it is not affected by changes in either light intensity or eccentricity of the stimuli and it has been suggested that what is actually transmitted from one hemisphere to the other is a motor command [1, 6, 10, 18]. Posterior areas, including the peristriate belt, are connected to ipsilateral premotor and prefrontal regions through long intrahemispheric bundles, the fasciculus longitudinalis superior of the old anatomists [8]. This anatomical arrangement allows fast transmission of information from the visual system of the hemisphere receiving the stimulus to the ipsilateral premotor area, and hence, through callosal fibers, to the premotor and motor areas of the contralateral hemisphere which performs the response (see Fig. 3).

Following this model of interhemispheric communication, in the crossed condition the information must run a long way within the damaged hemisphere before the callosal transfer occurs, and therefore intrahemispheric transmission is expected to be particularly vulnerable to the effect of an unevenly placed lesion. The correlation between lesion volume and CUD found in LBD patients supports this argument. On this assumption the abnormally long CUDs of brain-damaged patients may be viewed as reflecting the impaired *intrahemispheric* transmission rather than the *interhemispheric* transit time. What is unclear is whether in such a condition the information still travels through the damaged pathway or through alternative visuomotor connections. Acallosal and commissurotomized patients employ non callosal pathways for crossed responses. Clarke and Zaidel have proposed three alternative crossed visuomotor routes: the interhemispheric transfer of visual information through the anterior commissure, the interhemispheric subcallosal pathway involving superior colliculi and the ipsilateral motor pathway [10]. It is not known whether in patients with lesions acquired during the adult life these connections still are or may become effective, but on theoretical grounds they are a reasonable possibility. Some recent PET evidence, for instance, has been presented in favor of the idea that finger movements may be subsumed by the ipsilateral hemisphere [9].

Whatever the reason for the delayed CUD, this interpretation fails to explain the lengthening of CUDs observed in deeply located lesions (CUD in subcortical lesions = 12 msec.), since damage to the basal structures of the brain is not expected to affect transmission in more superficial bundles. As a a matter of fact the hypotheses so far discussed rest on the assumption that the stage of stimulus detection is equally effective in both visual fields. The detection of a visual stimulus implies prior focusing of attention on the stimulus itself [20], and this stage of the information pro-

cessing is assumed to be unimpaired both in acallosal, in brain bisected patients and obviously in normal people. However, in brain-damaged patients it may well not be so, and indeed there is ample evidence in the literature that unilateral brain lesions can affect the mechanisms of orienting attention when they are placed at different stages along the cortico-subcortical loops implied in attention orienting mechanisms [7, 16, 23]. In particular parietal lesions at the cortical level and thalamic lesions at the subcortical stage are especially important in disrupting contralateral attentional shifts, with the result that that the patient tends to overlook stimulation coming from the contralateral side in favor of the ipsilateral side. This has been found even in the absence of overt clinical signs of hemineglect, both in thalamic and in parietal lesions [13, 21, 22]. Therefore, if unilateral lesions produce a systematic trend of attentional shift away from the contralateral hemifield, or alternatively, a difficulty in engaging attention in the contralateral field, as Rafal and Posner have suggested for thalamic lesions [22], the RT to contralateral stimuli is expected to be slower than to ipsilaterally presented stimuli, especially so when the stimulus side changes randomly. Consistent with this view is the trend for CUDs to increase from the blocked to the random presentations. The experimental setup, with only one responding hand, may have further favored the attentional shift towards the ipsilateral side. In summary, at least in parietal and subcortical lesions, the CUD may be abnormally high as a result of attentional displacement rather than a consequence of intrahemispheric delayed transmission.

In conclusion, a unilateral cerebral lesion increases the CUD. This increase is probably related to more than one mechanism: the impairment of the intrahemispheric transmission of information is the first and more obvious candidate. In this case the CUD reflects either malfunctioning of the damaged occipito-frontal connections or less effective transmission along alternative interhemispheric pathways. Another possibility is that attentional factors provoke a bias towards the ipsilateral field. In this case the CUD reflects a functional imbalance in the readiness to respond to lateralized stimuli.

The various mechanisms are not mutually exclusive. Indeed their effects may be cumulative, depending on size and site of the lesion.

Sommario

In 39 pazienti portatori di una singola lesione cerebrovascolare emisferica (in 20 all'emisfero destro, in 19 all'emisfero sinistro), è stato effettuato un test di tempi di reazione semplici a uno stimolo visivo non strutturato presentato nel campo visivo ipsilaterale o controlaterale alla lesione. Le risposte erano effettuate sempre con la mano ipsilaterale.

La differenza fra tempi di reazione crociati (cioè stimolo e risposta su lati opposti) e tempi di reazione non-crociati (cioè stimolo e risposta dallo stesso lato) rappresenta il tempo di transito callosale dell'informazione e nei soggetti normali è dell'ordine di 3-5 msec.

Nei pazienti con lesione cerebrale tale valore era allungato a 20 msec di media, con un ulteriore ritardo a 37 msec. nei pazienti con lesione parietale. Non vi era nessuna differenza significativa fra pazienti con lesione dell'emisfero destro e pazienti con lesione dell'emisfero sinistro. La differenza fra risposte crociate e risposte dirette da noi trovata nei cerebrolesi è dello stesso ordine di grandezza di quella che presentano i soggetti con agenesia del calloso o i pazienti sottoposti a callosotomia.

Tuttavia, è verosimile che nei nostri pazienti il ritardo trovato rifletta piuttosto la somma di un'anomala conduzione intraemisferica e di possibili disturbi attenzionali.

Address reprint requests to:
Dr. G. Paolo Anzola
Clinica Neurologica dell'Università
II Divisione di Neurologia
P.le Spedali Civili 1
25125 Brescia

References

[1] ANZOLA G.P., BERTOLONI G., BUCHTEL H.A., RIZZOLATTI G.: *Spatial compatibility and anatomical factors in sample and choice reaction time.* Neuropsychologia 15:295-402, 1977.

[2] ANZOLA G.P., VIGNOLO L.A.: *Simple reaction time to lateralized visual stimuli is not related to the hemispheric side of lesion.* Cortex 1992, in press.

[3] BASSO A., CAPITANI E., LAIACONA M.: *Raven's Coloured Progressive Matrices: normative values on 305 adult normal controls.* Functional Neurology 2:189-194, 1987.

[4] BENTON A.L.: *Reaction time in brain disease: some reflections.* Cortex 22:129-140, 1986.

[5] BENTON A.L.: *Judgment of line orientation.* In A.L. Benton and K. de Hamsher (Eds.) *Contributions to neuropsychological assessment.* New York, Oxford: Oxford University Press, 1983.

[6] BERLUCCHI G.: *Interhemispheric integration of simple visuomotor responses.* In: P.A. Buser and A. Rougeul-Buser (Eds.) *Cerebral correlates of conscious experience.* North-Holland, Amsterdam, pp. 83-94, 1977.

[7] BISIACH E., VALLAR G.: *Hemineglect in humans.* In: F. Boller and J. Grafman (Eds.) *Handbook of Neuropsychology.* Vol. 1. Amsterdam-New York-Oxford, Ch. 11, pp. 195-222, 1988.

[8] BRODAL A.: *Neurological anatomy in relation to clinical Medicine.* New York, Oxford: Oxford University Press, 1981.

[9] CHOLLET F., DI PIERO V., WISE R.J.S., BROOKS D.J. et al.: *The functional anatomy of motor recovery after stroke in humans: a study with positron emission tomography.* Ann. Neurol. 29:63-71, 1991.

[10] CLARKE J.M., ZAIDEL E.: *Simple reaction times to lateralized light flashes. Varieties of interhemispheric communication routes.* Brain 112:849-870, 1989.

[11] DE RENZI E., FAGLIONI P.: *Normative data and screening power of a shortened version of the Token Test.* Cortex 14:41-49, 1978.

[12] KAIZER F., KORNER-BITENSKY N., MAYO N. et al.: *Response time of stroke patients to a visual stimulus.* Stroke 19:335-339, 1988.

[13] LADAVAS E.: *Is the hemispatial deficit produced by right parietal lobe damage associated with retinal or gravitational coordinates?* Brain 110:167-180, 1987.

[14] MARZI C.A., BISIACCHI P., NICOLETTI R.: *Is interhemispheric transfer of visuomotor information asymmetric? Evidence from a meta-analysis.* Neuropsychologia 29:1163-1177, 1991.

[15] MAZZOCCHI F., VIGNOLO L.A.: *Computer assisted tomography in neuropsychological research: a simple procedure for lesion mapping.* Cortex 14:136-144, 1978.

[16] MESULAM M.M.: *A cortical network for directed attention and unilateral neglect.* Annals of Neurology 10:309-325, 1981.

[17] MILNER A.D.: *Chronometric analysis in neuropsychology.* Neuropsychologia 24:115-128, 1986.

[18] MILNER A.D., LINES C.R.: *Interhemispheric pathways in simple reaction time to lateralized light flash.* Neuropsychologia 20:171-179, 1982.

[19] OLDFIELD R.C.: *The assessment and analysis of handedness: The Edinburgh inventory.* Neuropsychologia 9:97-113, 1971.

[20] POSNER M.I.: *Structures and functions of selective attention.* In Thomas Boll and Brenda Bryant (Eds.) *Clinical Neuropsychology and Brain Function: Research, Measurement and Practice.* American Psychological Association, pp. 171-202, 1989.

[21] POSNER M.I., WALKER J.A., FRIEDRICH F.J., et al.: *Effects of parietal injury on covert orienting of attention.* The Journal of Neuroscience 4:1863-1874, 1984.

[22] RAFAL R.D., POSNER M.I.: *Deficits in human visual spatial attention following thalamic lesions.* Proc. Natl. Acad. Sci. USA 84:7349-7353, 1987.

[23] RIZZOLATTI G., GALLESE V.: *Mechanisms and theories of spatial neglect.* In F. Boller and J. Grafman (Eds.) *Handbook of Neuropsychology* Vol. 1. Amsterdam-New York-Oxford, Ch. 12, pp. 223-246, 1988.

[24] TASSINARI G., MORELLI M., BERLUCCHI G.: *Interhemispheric transmission of information in manual and verbal reaction-time tasks.* Human Neurobiology 2:77-85, 1983.

[25] TOMASCH J.: *Size, distribution and number of fibres in the human corpus callosum.* Anat. Rec. 119:119-135, 1954.

[26] VIGNOLO L.A.: *The anatomical and pathological basis of aphasia.* In F. Clifford-Rose, R. Whurr and M.A. Wyke (Eds.) *Aphasia.* Whurr Publishers, London-Jersey City, p. 233, 1989.