Behavioural Neurology (1992), 5, 43-46

Interhemispheric transfer in Down's syndrome

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Callosal agenesics and callosotomized epileptics manifest markedly increasing simple visual reaction time (SVRT) from conditions of ipsilateral to contralateral stimulus-response relation (SRR). In the contralateral SRR, a response is presumed possible because of presence of other commissures (anterior, intercollicular). The SRR effect is prolonged presumably because the remaining commissures are less efficient than the corpus callosum in relaying necessary visual or motor information. Consequently, the SRR effect is believed to correspond to callosal relay time (CRT) in the normal subject. However, both callosal agenesics and callosotomy patients manifest general slowing of SVRT in addition to a prolonged SRR effect. These patients have massive extra-callosal damage which could plausibly cause both the SVRT and the CUD prolongation. If such were the case, the CRT inference would be in jeopardy. A test of the CRT inference is therefore required where patients with massive diffuse extra-callosal brain damage and normal callosi would show marked general SVRT prolongation and a normal SRR effect. Four trisomy-21 (T21) males were compared to age and sex-matched normal controls. General SVRT was highly significantly prolonged in T21, but the CUD was nearly identical in both groups.

INTRODUCTION

Over 50 published studies have been designed to investigate the difference between simple visual reaction time (SVRT) to targets ipsilateral versus contralateral to the responding hand, in normal humans. The difference between the two conditions has been termed, uncommittedly, the crossed-uncrossed differential or CUD (Zaidel, 1983), or more adventurously, interhemispheric transfer time or ITT (Bashore, 1981). In all of the reports reviewed by us, the condition requiring interhemispheric relay, namely the contralateral stimulus-response relation (SRR condition), always generated, on the average, a longer SVRT than the condition not requiring (in principle) any interhemispheric relay (ipsilateral SRR). A similar effect was always visible in the error ratios, suggesting to some authors (Zaidel, 1983) further evidence of an interhemispheric relay effect. Furthermore, callosal agenesics (Ettlinger *et al.*, 1972; Kinsbourne and Fisher, 1971; Lines, 1984; Milner *et al.*, 1985; Clarke and Zaidel, 1989) and callosotomized epileptics (Smith, 1947; Sergent and Myers, 1985) manifest SVRT-CUDs which are markedly prolonged compared to those of normal subjects. It has been presumed that in these cases, in the contralateral SRR, a response is possible because of the presence of other interhemispheric commissures such as the anterior or intercollicular commissures. It has also been concluded that CUDs in these cases are prolonged because the remaining commissures are less efficient than the corpus callosum in relaying such visual or motor information in such tasks. Consequently, it is commonly believed that the CUD is an index of callosal relay time (CRT) in the normal subject.

However, both callosal agenesics and callosotomy patients manifest general slowing of SVRT in addition to prolonged CUDs. For different reasons and in different ways (foetal hypoplasic brain development, post-natal progressive degenerative brain disease, etc.) these patients have relatively massive and diffuse extra-callosal damage in addition to not having a callosal commissure. The extra-callosal damage could plausibly be the sole or major cause of both the SVRT and CUD prolongation, rather than only of general SVRT. If this were to be the case, the ITT (or CRT) inference from SVRT would be in jeopardy.

To help consolidate the SVRT-ITT inference it would therefore be useful to demonstrate that massive diffuse extra-callosal brain damage (not affecting the corpus callosum) can heavily prolong general SVRT while leaving unaffected the CUD. Down's syndrome provides an interesting exemplar of the preceding requirements. The disease results from trisomy of the 21st chromosome group, involves primarily post-natal dendritic hypoplasia and heterotopia involving the entire cortex and subcortical grey matter, cerebellum and brain stem, and premature cortical and hyppocampal aging—including Alzheimer-disease type neuropathology from the second decade on. Surprisingly and remarkably, there is normal white matter organization, normal myelinization and a normal-looking corpus callosum (see Kemper, 1988, for a detailed review).

TABLE I. Outline of simple visual reaction time (SVRT) and the crossed-uncrossed differential (CUD) of published cases of callosal agenesis, callosotomy and of a selection of recently published normal group average results

Reference	Case	SVRT	CUD
Callosal agenesics			
Clarke and Zaidel, 1989	M.M.	362	22.1
Ettlinger *et al.*, 1972	G.D.	461	13.6
Kinsbourne and Fisher, 1971	S.F.	245	18.3
Lines, 1984	K.C.	340	23.4
Milner *et al.*, 1985	B.F.	312	13.2
Callosotomized epileptics			
Sergent and Myers, 1985	LB	350	40.1
Sergent and Myers, 1985	NG	350	40.3
Smith, 1947	GD	450	22.1
Groups of normal subjects			
Clarke and Zaidel, 1989	GD	309	1.9
Levy and Wagner, 1984	GD	215	2.0
Lines and Milner, 1983	GD	288	2.3
Lines *et al.*, 1984	GD	258	1.7
Rizzolatti, 1979	GD	229	1.5
Saron and Davidson, 1989	GD	256	10.3
St John *et al.*, 1987	GD	257	5.0
Tassinari *et al.*, 1983	GD	193	2.9

GD, group data.

METHOD

Subjects

Four subjects with karyotype-documented Down's syndrome (T-21) were recruited from a residential shelter. Four age and sex-matched normal subjects served as controls. All subjects were male and right handed. See Table II.

TABLE II. Biographic and clinical description of the subjects

Group	ID	Age	Education	IQ
Trisomy (21)	1	19	—	38
	2	16	—	45
	3	16	—	40
	4	18	—	43
Normal control	1	19	12	—
	2	17	12	—
	3	20	15	—
	4	21	15	—

Procedure

A simple reaction time paradigm was implemented on an Apple IIe computer with an Applied Engineering timing card and an Amdek video monitor. Stimuli consisted of 1 square-cm white squares (636 cd/m^2 luminance) on a black background (20 cd/m^2). These measures were obtained with a Quantum Instruments Photo-Meter-I fitted with a PM-10 fiber optic probe designed for directly measuring brightness of small areas of video screens. The experiment was carried out in a dimly lit room (52 foot-candles). This measure was obtained using another probe designed for capturing illuminance from all angles within a 180 degree hemisphere. All stimuli were presented to the right or left of center screen at 11 arc degrees (4.5 cm) of eccentricity (defined in terms of center to the inner edge of the stimulus). Subjects' foreheads rested against a stopper at 50 cm from the screen and the subject's eyes were at center screen level. Targets were of a dimension of 2.5 arc degrees. A red light-emitting diode (LED) was "on" throughout the entire experiment, was placed at center screen, and served as a fixation point. Stimulus duration was 140 ms (± a 16 ms variation intrinsic to computer-generated video-display stimuli). The experimental routine proceeded as follows. After the experimenter provided standard instructions, the computer ran a series of 40 trials followed by a 2 min rest period. The subject was required to immediately press the middle of the space bar of the keyboard with his index finger as soon as he detected the stimulus. The responding finger was 25 cm in front of the subject's body midline on a table. Each subject responded with the same hand throughout each run. Immediately after the response, the RT was displayed at the bottom-screen (500 ms) or a message indicated that an excessive delay (> 2000 ms) or an anticipation (RT < 75 ms) had resulted in cancellation and replacement, to come, of the trial. Each cancelled trial was replaced by another trial resulting in 40 valid trials in each run. Feedback was presented to "shape out" response biases (anticipations, delays) and to motivate the subjects to maintain attention by attempting to improve their response speeds. After the feedback disappeared, an interval of 1050, 1150, 1300 or 1500 ms of black screen occurred. Each such interval was equiprobable and randomly distributed. Subjects were instructed to look at the feedback and then immediately fixate the LED. Hemilocation of stimuli was equiprobable and pseudo-random. Maximum repetition in a hemifield was three. Two subjects in each group started with the left hand, while two started with the right hand. On each subsequent "run" of 40 trials the responding hand was alternated. Each subject completed four "runs" of 40 trials. In all, each subject therefore produced 160 valid RTs.

The computer program tabulated RTs into each cell of the design and computed medians. In addition, both types of errors (anticipation and delays) were tabulated in terms of frequency in each cell of the design. However, only delay errors (omissions) were retained for further presentation and analysis.

TABLE III. Omission errors (> 2 s) by each subject in each field and hand condition, and according to group (trisomy-21 vs. normal control)

Group	ID	RH RF	RH LF	LH LF	LH RF
T21	1	8	17	9	10
T21	2	25	23	25	22
T21	3	73	52	47	50
T21	4	12	16	13	20
Total		118	108	94	102
NC	1	0	4	1	1
NC	2	1	6	6	2
NC	3	0	1	0	0
NC	4	1	0	1	0
Total		2	11	8	3

T21, trisomy-21; NC, normal control; L, left; R, right; H, hand; F, field.

TABLE IV. Median reaction times (ms) by each subject in each field and hand condition, and according to group (trisomy-21 vs. normal control)

Group	ID	RH RF	RH LF	LH LF	LH RF
T21	1	969	958	874	822
T21	2	638	738	729	670
T21	3	1195	1186	1156	1257
T21	4	563	541	529	486
Mean		841	856	823	809
NC	1	291	284	277	280
NC	2	196	203	205	210
NC	3	260	274	257	267
NC	4	249	253	239	223
Mean		249	253	244	245

T21, trisomy-21; NC, normal control; L, left; R, right; H, hand; F, field.

RESULTS

Errors

The T-21 subjects made more than 17 times more errors than the normal control subjects (Chi square goodness of fit test: $\chi = 355.16$, $p < 0.0000$). There were sufficient error frequencies at each hand and in each field in the T-21 data to support a Chi square test of independence—amounting to a test of the FIELD × HAND interaction or CUD. The interaction was indeed significant (Chi square test of independence: $\chi = 4.69, p < 0.05$. The normals did not make enough errors to support statistical analysis but group data suggest presence of a CUD (see Table III).

Reaction times

The median RTs were subjected to a $2 \times 2 \times 2$ repeated measures ANOVA. The within factors were FIELD and HAND and the between factor was GROUP. Only the between main effect reached statistical significance ($p < 0.007$), the effect consisting of the T-21 subjects having RTs more than 3.5 times longer than the normal controls. The CUDs of the T-21 and NC groups were 0.7 and 2 ms, respectively. These values are in the normal range as can be seen in Table I. The RT data are presented in Table IV.

DISCUSSION

The findings unequivocally support the inference according to which CUDs drawn from SVRT are, or closely reflect, ITT and perhaps even CRT. Indeed, not only are SVRT and resultant error-CUDs always positive in the experiments previously and presently published, but there are now good grounds for believing that congenital or surgical loss of the corpus callosum is the sole cause of prolongation of CUDs, and not the accompanying extra-callosal diffuse damage. In short, it now seems all the more likely that CUDs drawn from SVRT reflect ITT, and that the corpus callosum may indeed be one of the more efficient interhemispheric commissures supporting the relay imposed by such tasks.

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