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Relationship between crossover and modality shift effects in sequential reaction time performance of schizophrenic patients

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Summary. On the basis of reaction time measurement, two well-known experimental indicators of attentional dysfunctions in schizophrenia were studied. These are the crossover effect (COE), induced by alternating preparatory intervals, and the modality shift effect (MSE), induced by alternating stimulus modalities. For the first time, the relationship between these indicators was examined. Correlations of both indicators with clinical variables such as psychopathology, subjective complaints, duration of illness and medication were also analyzed. Subjects were 50 schizophrenic inpatients and 50 healthy controls, 21 women and 29 men in each group. While earlier results for COE and MSE were replicable, no correlation between the two was found, leading to the conclusion that they involve different aspects of attention not necessarily impaired to the same extent in all patients.

Key words: Schizophrenia – Reaction time performance – Crossover effect – Modality shift effect

Introduction

Measurement of reaction time, particularly in sequential reaction time tasks, is a highly effective method to explore attentional dysfunctions in schizophrenic patients (Nuechterlein 1977; Nuechterlein and Dawson 1984). As early as the 1930s, the classic task of this type, the Shakow paradigm, led to the discovery of a characteristic response pattern in schizophrenic patients. According to this paradigm, in a continuous series of trials the time interval between a warning signal and an imperative signal, the so-called preparatory interval (PI), is either constant (regular PI series) or variable (irregular PI series). Normals profit from regularity for PIs up to 25 s, i.e. response latencies are shorter for regular than for irregular conditions. Schizophrenics show this advantage only with short PIs. With PIs longer than about 3 s, they frequently show longer reaction times in regular than in irregular series (Huston et al. 1937; Rodnick and Shakow 1940). This finding, termed the 'crossover effect' (COE), is generally interpreted as indicating a disturbance of maintenance of attention (i.e., a deficit in readiness to respond) as a result of set-segmentalization, i.e. a breakdown of task relevant "generalized" or "major sets" caused by minor or irrelevant aspects of the stimulus/response process (Shakow 1962, 1977; for alternative explanations, see Bellissimo and Steffy 1972; Steffy and Galbraith 1974; Borst and Cohen 1987).

An important modification of the COE task was introduced by Bellissimo and Steffy (1972). In their 'embedded set procedure', as opposed to the classical 'long run procedure' described above, they no longer presented regular vs. irregular PI series in separate blocks of trials. Instead they inserted runs of four PIs of equal length ('isotemporal blocks') within generally irregular series. Studies using the embedded set procedure have demonstrated a differential COE more consistently than studies using the long run procedure (Jahn 1991). Therefore we decided to adopt the embedded set procedure instead of the classical long run procedure for the purposes of our study, in spite of an ongoing discussion about the comparability of the two task versions, especially in view of PPI (preceding preparatory interval) × PI interactions (e.g., Galbraith et al. 1983; Strauss and Wagman 1988; for a summary of the discussion, see Rist and Cohen 1991).

In another sequential reaction time task, the Sutton-Zubin paradigm, light and tone stimuli are presented in random order as imperative stimuli requiring a fast motor response. Each response is classified according to the modality of the stimulus and whether this stimulus has been preceded by a signal from the same (ipsimodal) or the other (crossmodal) modality. Even in the first study of this type (Sutton et al. 1961), it was evident that retardation of reaction time under crossmodal conditions was much more pronounced among schizophrenic patients than healthy controls. This 'crossmodal retardation' (CMR) or differential 'modality shift effect' (MSE), was regarded as evidence for a disturbance in shift of atten-

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tion (Zubin 1975). The theoretical assumptions have been further refined by Rist and Cohen (1987).

Both reaction time effects have been replicated many times (Rist and Cohen 1991; Jahn 1991). Surprisingly, no data are available about the relationship between the two sequential effects. More than a decade ago, Spring and Zubin stated "Perhaps experiments comparing the same individuals on both techniques, ...would help to clarify the similarities and differences between the components of attention measured by each task" (Spring and Zubin 1977, p. 443 f.).

Following Spring and Zubin (1977; also see Spring 1980; Cohen et al. 1985) we expected that the two effects tap different aspects of attention which are not necessarily impaired to the same extent in all patients. In addition, we wanted to study possible relationships between the performance of schizophrenic patients in the two reaction time tasks with clinical ratings of psychopathology and self-reports of the patients. Most previous studies have reported only negligible correlations (Cancro et al. 1971; Cohen et al. 1984; DeAmicis and Cromwell 1979; Mannuzza et al. 1984; Oldings 1985; Spaulding et al. 1984; Strauss et al. 1979). Finally, we wanted to take into account possible influence of neuroleptic medication, although there is empirical evidence that these agents either do not affect reaction time performance or, if so, influences are in the direction of normalization of performance (for an overview, see Spohn and Strauss 1989).

Subjects and methods

Subjects

A total of 118 subjects participated in the study, 55 psychiatric patients and 63 healthy controls. All subjects gave informed consent to participation. Five patients were excluded from the study for technical reasons or due to later change in diagnosis. The remaining 50 patients were matched with 50 healthy controls for age and gender. Table 1 provides a list of the sample characteristics.

All patients were receiving inpatient treatment at the Central Institute of Mental Health, Mannheim, at the time of testing. Diagnoses were made by consensus between two psychiatrists according to ICD 9. Patients with any known instances of organic brain disease and alcohol or drug dependency were exlcuded. Categorization of patients acording to subgroups of schizophrenia yielded the following results: 35 cases of paranoid-hallucinatory schizophrenia (295.3), eight residual schizophrenia (295.6), three schizoaffective psychoses (295.7), two cases of hebephrenia (295.1), one schizophrenia simplex (295.0) and one acute schizophrenic episode (295.4). At the time of testing nine patients had been free of neuroleptic medication for at least two weeks. The group of healthy controls included students, scientific and administrative personnel of the University of Mannheim as well as members of the clinical staff.

Following the concept of "basic symptoms" (Süllwold and Huber 1986) self-experience of psychological deficits and anhedonia were determined by means of a self-assessment questionnaire (Complaints Questionnaire; Langer et al. 1985), combining items from the following instruments: the Scales for Physical and Social Anhedonia (Chapman et al. 1976), the Perceptual Aberrations Scale (Chapman et al. 1978), the Hoffer Osmond Diagnostic Test (Kelm et al. 1979), and the Frankfurt Complaints Questionnaire (Süllwold 1981). As expected, patients reported more basic symptoms ($P < 0.001$) and anhedonia ($P < 0.0001$) than normal controls (see Table 1), according to the Mann-Whitney U-test. Clinical ratings of psychopathology were determined using the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962) and the Nurses' Observation Scale for Inpatient Evaluation (NOSIE; Honigfeld et al. 1976). Neuroleptic medication was calculated in chlorpromazine equivalents (Jahn and Mussgay 1989).

Table 1. Means and ranges of sample characteristics

	Patients	Controls
Male : Female	29 : 21	29 : 21
Age (years)	30.1	29.6
	18–47	20–51
Level of education		
low	26	5
medium	10	3
high	14	42
Complaints questionnaire[a]	14.0	4.6
Basic symptoms	0–43	0–14
Complaints questionnaire[a]	5.5	2.3
Anhedonia	0–12	0–7
Brief Psychiatric Rating Scale	40.9	
Total score	22–69	
Nurses' Observation scale[b]	208.6	
Index score	122–238	
Duration of illness	51.8	
(month)	0–276	
Number of hospitalizations	3.9	
	1–25	
Total duration of	7.7	
hospitalization (month)	0–35	
Neuroleptic medication	213.5	
(chlorpromazine equivalents)	0–930	

[a] Calculated from 36 patients and 49 controls
[b] Calculated from 33 patients

Experimental procedures

The two reaction time tasks were carried out in the same experimental session together with an electrodermal habituation study not reported here. Total duration was 45–50 min. The order of testing was always the same (electrodermal habituation task, COE task, MSE task). Simple response latencies were measured in milliseconds using the computer-based Mannheim Stimulus Response Device (Maus Co./Ludwigshafen). COE was studied according to the embedded set procedure (Bellissimo and Steffy 1972). The warning signal was a 1000-Hz tone, the imperative signal a 500-Hz tone, each with a SPL of 60 dB and a duration of 150 ms. Subjects were asked to press a key as quickly as possible to the imperative signal. Preparatory intervals (PI) between the warning and the imperative stimuli varied from 1 to 8 s. The intertrial intervals were all of the same duration (1.5 s). Trials with PIs of 1, 3 and 7 s duration were selected for analysis. Each duration followed every other duration an equal number of times. The signal series consisted of a total of 130 trials, of which the first 10 were excluded from data analysis.

For the MSE, a 500-Hz tone and a red light, both with a duration of 150 ms, served as imperative stimuli. Intertrial intervals

varied randomly between 1.0 and 1.5 s. Signals from both modalities varied randomly over a total of 63 trials. The first 10 trials were excluded from analysis, as were five crossmodal reactions after a triple repetition of stimuli from the same modality.

Data analysis

The COE task was analyzed in a three-way ANOVA with subject group (patient vs. control) as a between-factor, and preparatory interval (1 vs. 3 vs. 7 s) and regularity (regular vs. irregular) as repeated measurement factors. Similarly, the MSE task was analyzed in a three-factor design with modality (visual vs acoustic) and sequence (ipsimodal vs. crossmodal) as the two repeated measurement factors. Medians of reaction times under each experimental condition were determined for each subject as the dependent variables. An epsilon-corrected F-test (Greenhouse-Geisser) was used to evaluate the significance of main effects and interactions. In addition, the following indices were determined: 1. average median reaction time for both tasks (RT_{mean}); 2. the difference between the median latencies from regular and irregular conditions for trials with the longest preparatory interval in the COE task ($COE = RT_{7\,sec/reg} - RT_{7\,sec/irr}$); 3. the difference between the medians for cross- and ipsimodal trials in the MSE task, separately for tone and light stimuli (MSE_{tone}, $MSE_{light} = RT_{cross} - RT_{ipsi}$).

Results

Sequential reaction time effects

A three-way analysis of variance of the median reaction time from the COE showed significant main effects for all three factors (group: $F(1,98) = 35.3$; $P < 0.0001$; regularity: $F(1,98) = 29.2$; $P < 0.0001$; interval: $F(2,196) = 15.7$; $P < 0.0001$) as well as significant interactions group × interval ($F(2,196) = 6.7$; $P < 0.002$), regularity × interval ($F(2,196) = 71.4$; $P < 0.0001$) and group × regularity × interval ($F(2,196) = 9.5$; $P < 0.0002$). As can be seen in Fig. 1, schizophrenics had generally longer reaction times and exhibited a marked COE, in contrast to the healthy controls. Only the schizophrenics show a statistically significant difference between regular and irregular 7-s PIs ($F(1,196) = 8.8$; $P < 0.01$), with longer reaction times for the regular trials. The difference is negligible in healthy controls ($F(1,196) = 0.6$; n.s.).

The three-way analysis of variance for the MSE also resulted in significant main effects for all three factors

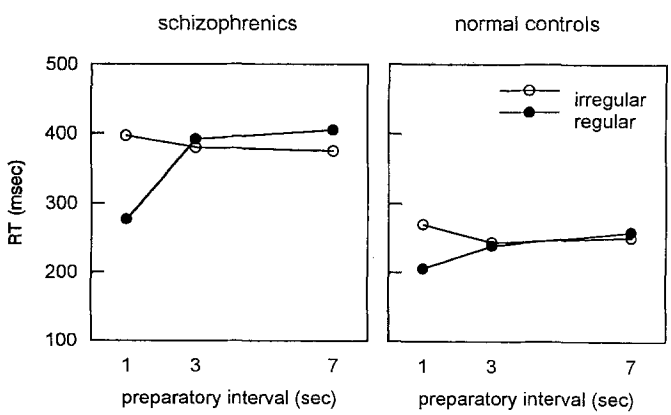

Fig. 1. Mean reaction time performance of schizophrenics ($n = 50$) and normal controls ($n = 50$) in response to variable preparatory intervals under regular and irregular conditions (COE task)

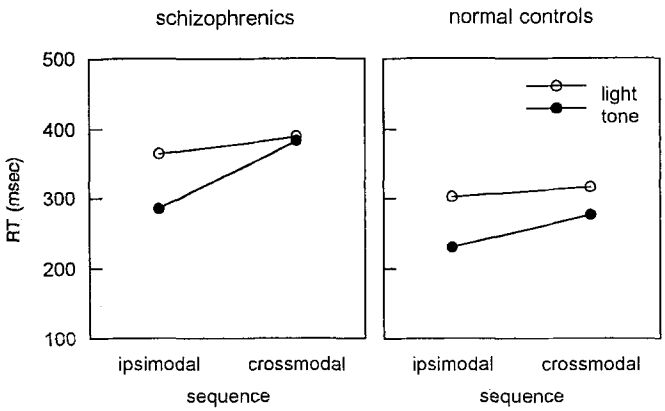

Fig. 2. Mean reaction time performance of schizophrenics ($n = 50$) and normal controls ($n = 50$) in response to ipsimodal vs crossmodal sequences of tone and light stimuli (MSE task)

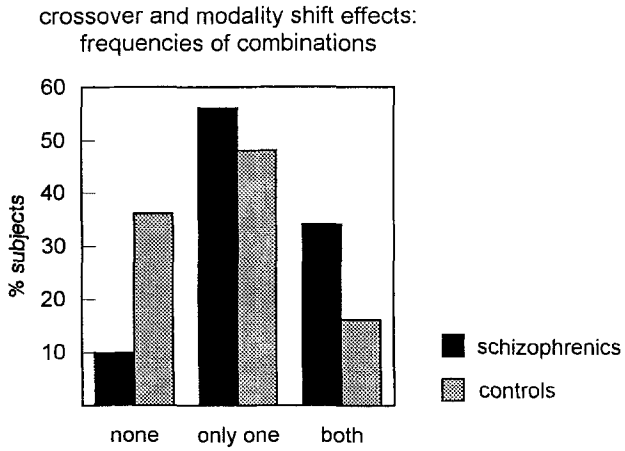

Fig. 3. Relative frequencies of schizophrenics and normal controls without, with one, and with both sequential reaction time effects

(group: $F(1,98) = 17.5$; $P < 0.0001$; modality: $F(1,98) = 91.8$; $P < 0.0001$; sequence: $F(1,98) = 98.9$; $P < 0.0001$), as well as significant interactions for group × sequence ($F(1,98) = 11.4$; $P < 0.002$), modality × sequence ($F(1,98) = 51.8$; $P < 0.0001$), and group × modality × sequence ($F(1,98) = 8.8$; $P < 0.004$). For both groups, comparisons between ipsi- and crossmodal reaction times confirm the crossmodal retardation in response to tones (schizophrenics: $F(1,98) = 176.4$; $P < 0.001$; controls: $F(1,98) = 38.1$; $P < 0.001$), while crossmodal retardation in response to light stimuli is less pronounced in both groups and statistically significant only for the patients (schizophrenics: $F(1,98) = 9.8$; $P < 0.01$; controls: $F(1,98) = 3.7$; n.s.).

Relationship between COE and MSE

Apart from the expected relationship between the average reaction times in both tasks (schizophrenics $r = 0.70$; $P < 0.001$; controls $r = 0.63$; $P < 0.001$), no significant correlations were found between the indices for the sequential reaction time effects: the COE index correlated with the MSE index for tone stimuli $r = 0.24$ in schizophrenics and $r = 0.18$ in controls, with the MSE index for light

Table 2. Spearman rank correlations between measures of reaction time performance and psychopathology

	Crossover task		Modality shift task		
	RT_{mean}	COE	RT_{mean}	MSE_{tone}	MSE_{light}
Brief Psychiatric Rating Scale[a]					
Anxiety/Depression	0.17	0.04	0.01	0.03	−0.05
Anergia	0.29*	−0.10	0.33*	0.16	0.23
Thought disturbance	0.34*	0.07	0.29*	0.07	−0.12
Activation	0.20	−0.07	0.19	0.06	0.00
Hostility/suspiciousness	0.20	0.11	0.05	−0.04	−0.19
Total score	0.36**	0.07	0.25	0.10	−0.02
Nurses' Observation Scale[b]					
Index score	−0.14	−0.10	−0.06	−0.31	−0.12
Complaints Questionnaire[c]					
Basic symptoms	0.16	0.19	0.20	0.26	0.00
Anhedonia	0.40*	−0.07	0.42**	0.44**	0.16

[a] Calculated from 50 patients
[b] Calculated from 33 patients
[c] Calculated from 36 patients
*$P < 0.05$; **$P < 0.01$ (two-tailed, no alpha adjustment)

stimuli $r = -0.17$ in schizophrenics and $r = -0.14$ in controls.

Following the suggestions of Cromwell (1975; DeAmicis and Cromwell 1979), we applied a cut-off of 25 ms difference between regular and irregular trials to decide whether or not a subject exhibited an individual COE. The same criterion proved optimal (i.e., was most discriminative between groups) for the acoustic MSE.

As illustrated in Fig. 3, while 17 of the schizophrenics, but only 8 of the normals showed both effects, only 5 schizophrenics, but 18 controls showed none of the effects. The frequencies with which the different combinations of effects occurred in both groups differ significantly (chi-square = 10.9; $P < 0.01$).

Relationships between measures of reaction time performance, psychopathology and neuroleptic medication

Within the group of schizophrenics, Spearman rank correlations were calculated between measures of reaction time performance and clinical variables. Duration of illness correlated $r_S = 0.32$ ($P < 0.05$) with average reaction time in the MSE task, but not in the COE task ($r_S = 0.20$; n.s.). Correlations between duration of illness and reaction time effects ranged from −0.04 to 0.27, none reaching significance.

As can be seen from Table 2, mean reaction times correlated to some extent with psychopathological symptoms. In contrast, sequential reaction time effects are largely independent of psychopathology, with one notable exception: crossmodal retardation to tone stimuli is positively correlated with anhedonia as measured by questionnaire, and negatively with the overall adjustment of ward behavior according to nurses ratings (i.e., better functioning subjects showed less crossmodal retardation). The latter correlation is not quite significant at the 5% level because of reduced sample size.

Of the five correlations calculated between chlorpromazine equivalents of neuroleptic medication and reaction time indices, four ranged between −0.10 and 0.03. The fifth indicated a significant relationship between medication and COE ($r_S = 0.29$; $P < 0.05$). Comparing the nine patients who were off medication at the time of testing with nine patients who received the highest chlorpromazine equivalents (mean = 538.8, range = 348.0–930.0; six men and three women in each subgroup), no differences could be seen for the MSE. In the COE task patients without neuroleptic medication had longer reaction times, while the difference between regular and irregular trials was larger in those with the highest dosages. Due to the small sample size, differences were not significant.

Discussion

The present study appears to be the first to investigate the correlation between the well-known sequential reaction time phenomena of crossover effect (COE) and modality shift effect (MSE). As could be expected, in both tasks the patients responded significantly slower than healthy controls, and exhibited stronger sequential reaction time effects. The especially strong acoustic (as opposed to visual) crossmodal retardation is also a frequently replicated finding; however, this 'channel specificity' seems to disappear when subjective intensities of acoustic and visual stimuli are matched (Mannuzza et al. 1984; Spring 1980; Waldbaum et al. 1975).

In our study, the crossmodal retardation following tone stimuli was statistically significant even in healthy controls. This is probably a result of the comparatively short intervals between stimuli (Oldigs and Rey 1982; Rey et al. 1987). According to the theory of neural trace persistence (Zubin 1975), one would predict a weaker differential MSE when intertrial intervals are short.

There were no substantial correlations between the indices defining the sequential reaction time effects. This result corresponds to many earlier findings of generally weak relationships between different attention tests used in schizophrenia research (e.g., Kopfstein and Neale 1972). The attention disturbances in schizophrenic patients as captured by the COE and MSE are independent phenomena. However, more schizophrenic patients exhibited both effects than healthy controls, and controls more often showed neither of the effects.

Mean reaction time performance in both tasks was positively correlated with certain aspects of psychopathology, in particular with the amount of anergia and thought disturbance, as rated by experts, and with self-experienced anhedonia. On the other hand, in agreement with most other studies, sequential reaction time performance of schizophrenic patients showed no substantial relationships with clinical variables (Cancro et al. 1971; Cohen et al. 1984; Oldigs 1985), apart from one exception. Crossmodal retardation in response to tone stimuli correlated positively with self-rated anhedonia and, at least to some extent, negatively with ward behavior, indicating that patients with lower values in social competence, social interest and personal neatness, and higher values in irritability, manifest psychosis, retardation and depression tend to show more crossmodal retardation. Also, when taking a closer look at psychopathology using BPRS items instead of subscores, MSE, but not COE showed weak correlations with symptoms such as emotional withdrawal ($r_S = 0.29$; $P < 0.10$), motor retardation ($r_S = 0.27$; $P < 0.10$) and blunted affect ($r_S = 0.26$; $P < 0.10$). Although not entirely consistent, these correlations are of special interest in view of an earlier investigation (Rey and Oldigs 1982), in which significant relationships between acoustic MSE and PSE subscore BSO (behavior, speech and other syndromes) as well as BPRS item 16 (blunted affect) were reported. Our results and those of Rey and Oldigs seem to indicate that MSE, while more or less independent of positive symptoms, may correlate to some extent with negative symptomatology.

In correspondence with previous studies (Spohn and Strauss 1989), no relationship between neuroleptic medication and reaction time performance was found. In the task measuring MSE, nearly identical results were obtained in terms of average performance level and amount of crossmodal retardation, when patients with highest dosage were compared to those without medication. In the case of the COE, unmedicated patients even showed an increased overall reaction time level, while the COE itself seemed to be more pronounced in patients receiving highest dosages. In view of the small samples size, it should be noted that this could be an artifactual finding, because the patient with the smallest COE belonged to the nine patients without medication, while the subject with the largest COE belonged to the nine patients with maximal medication.

In conclusion, sequential reaction time abnormalities such as crossover and modality shift effects in schizophrenic patients are relatively independent of various clinical variables. Thus, these measures do not simply reflect current psychopathology or medication, but instead appear to be empirical indicators of subtle attentional dysfunctions in schizophrenia. On the other hand, the lack of any substantial relationship between COE and MSE points to the complexity of the underlying deficits in central information processing.

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