

Assessment of attention network efficiency in schizophrenic patients with positive and negative symptoms

Valutazione della performance dei network attentivi in pazienti schizofrenici con sintomi positivi e negativi

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SUMMARY. Aim. The aim of the present study was to examine the anterior (Experiment 1) and posterior (Experiment 2) attention systems in schizophrenic patients with predominantly negative or positive symptoms, in order to evidence possible differences in symptomatology. **Materials and methods.** The schizophrenic sample was divided into two subgroups: negative (n=13) versus positive symptoms (n=10). The anterior and posterior attention systems in schizophrenic patients were assessed through two experiments: a dual-task paradigm evaluating executive functions, in particular planning and coordination, and a Simon task evaluating automatic shifting of visual attention. **Results.** Our study showed specific attention deficits in the presence of negative symptoms. These findings suggest that negative schizophrenics have a deficit that affects functioning of both anterior and posterior attention systems, whereas positive schizophrenics showed a selective deficit only for the posterior attention system, with a pattern that is in the opposite direction compared to that of negative schizophrenics. **Discussion.** Our results demonstrate that specific symptom dimensions or patterns are associated with specific cognitive impairments. Notably, negative schizophrenics exhibited clear abnormalities, whereas positive schizophrenics performed very similarly to healthy controls.

KEY WORDS: schizophrenia, negative symptom, positive symptom, dual-task, Simon effect.

RIASSUNTO. Scopo. L'obiettivo del presente studio è di esaminare i sistemi attentivi anteriore (Esperimento 1) e posteriore (esperimento 2) nei pazienti schizofrenici con sintomatologia prevalentemente negativa o positiva, al fine di evidenziare differenze. **Materiali e metodi.** Il campione di schizofrenici è stato suddiviso in due gruppi: sintomatologia negativa (n=13) e positiva (n=10). I sistemi di attenzione anteriore e posteriore nei pazienti schizofrenici sono stati esaminati attraverso due esperimenti: il paradigma del doppio-compito valuta le funzioni esecutive, con particolare riguardo alla pianificazione e coordinamento e il Simon-task valuta il cambio automatico dell'attenzione visiva. **Risultati.** Il nostro studio dimostra l'esistenza di specifici deficit di attenzione in presenza di sintomi negativi. Questi risultati suggeriscono che gli schizofrenici negativi hanno un deficit che influenza il funzionamento del sistema attentivo anteriore e posteriore, mentre gli schizofrenici positivi mostrano un deficit selettivo solo per il sistema attentivo posteriore, con un pattern che è in direzione opposta rispetto a quello degli schizofrenici negativi. **Discussione.** I nostri risultati supportano l'idea che i patterns di determinati sintomi sono associati a specifici deficit cognitivi. Ciò che sorprende è che gli schizofrenici negativi manifestano anomalie evidenti, mentre quelli positivi eseguono in modo molto simile ai controlli sani.

PAROLE CHIAVE: schizofrenia, sintomi negativi, sintomi positivi, doppio-compito, effetto Simon.

INTRODUCTION

The positive/negative dichotomy of clinical symptoms of schizophrenia has a long history in phenomenological psychiatry (1). Positive and negative symptom dimensions have figured prominently in recent discussions of the pathogenesis and course of schizophrenia (2-4). The negative-positive distinction, first introduced into the psychiatric literature by Strauss et al. (5), has been further developed by Crow (2,6), who has proposed that there are two clinical syndromes involved in schizophrenia, one characterized by florid positive symptomatology (e.g., hallucinations and delusions) and by disturbances in dopaminergic transmission, and the other characterized by enduring negative symptomatology (e.g., apathy and flattened affect) and structural abnormalities of the brain. Crow further maintains that while the two syndromes reflect separate pathological processes, they do not constitute separate diseases, since they commonly occur together, either simultaneously or at different time points, with early positive episodes typically progressing to the more incapacitating negative defect state.

In spite of the central role of attention deficits in schizophrenia (6,7), relations between attention deficits and different symptom dimensions are still scarcely known (8,9). Previous studies have evidenced the existence of attentional deficits in the presence of negative symptoms (10-12), whereas several recent studies suggest that positive symptomatology may be related to the inhibitory components of selective attention (13,14).

Posner and Dehaene (15) divide the attention system into subsystems that perform different functions. The anterior attention system (prefrontal cortex, cingulate gyrus, and basal ganglia) serves executive functions and is involved in the attentional recruitment and control of brain areas to perform complex cognitive tasks. The posterior attention system (superior parietal cortex, pulvinar and superior colliculus) is responsible for selecting one stimulus location among many and for shifting attention to it.

There seem to be stable associations between specific aspects of schizophrenia and certain brain areas. In particular, it has been suggested that negative symptomatology is associated with dorso-lateral prefrontal cortex malfunctioning, whereas positive symptomatology is associated with basal orbito-frontal malfunctioning (16-18).

If each variety of schizophrenia were related to specific neuronal structures, then one would predict difficulties in replicating findings as the symptom/syndrome patterns displayed by patients vary across sam-

ples. This may account for some literature inconsistencies concerning neuropsychological anomalies associated with schizophrenia.

The aim of the present study was to assess the anterior (Experiment 1) and posterior (Experiment 2) attention systems in schizophrenic patients with predominantly negative or positive symptoms, in order to identify possible differences in symptomatology. Experiment 1 tested executive functions, with specific regard to planning and coordination, and Experiment 2 tested automatic shifting of visual attention.

All participants provided informed consent before participation in the study. Normal controls and patients meeting DSM-IV criteria for schizophrenia (19) participated in Experiments 1 and 2.

MATERIALS AND METHODS

Experiment 1: A dual-task paradigm

A paradigm that has proved very useful to study how executive functions operate is the one developed by Umiltà et al. (20). In it, two tasks must be executed and the execution sequence has to be coordinated, in order to execute one response after the other. The primary speeded task requires discriminating whether two stimuli are to the left or to the right of the fixation point. The secondary un-speeded task requires discriminating whether the two stimuli are same or different. Reaction time (RT) to the primary task is slower with than without the secondary task (i.e., a dual-task cost).

To explain the dual-task cost in normals, Umiltà et al. (20) adopted Pashler bottleneck notion (21,22) and proposed that the bottleneck occurs at the decision stage. In particular, they suggested that the decision to perform the two tasks one after the other competes for access to the same processing stage with the decision to execute the first response. This common stage acts as a bottleneck, causing postponement of the response to the primary task and lengthening of RT for this task. Therefore, the extra time needed to perform the primary task in the presence of the secondary task would be due to the coordination of the two tasks, that is to the instructions to perform the two tasks in a pre-specified order. Also, Umiltà et al. (20) argued that the structure in which the two responses are coordinated is the Supervisory Attentional System (SAS) (23,24) which is called upon when planning and decision-making strategies are required.

Subjects

Twenty-three patients and 17 normal controls participated in Experiment 1 (**Table 1**). All subjects with a gross brain disease, a significant history of drug and alcohol

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Table 1. Experiment 1: Demographic, clinical details and results in the dual task for the three groups (Negative and Positive Schizophrenics and Controls)

	Schizophrenic subjects		Controls n=17
	Negatives n=13	Positives n=10	
Age (years)	32.38 (4.51)	34.10 (6.19)	30.82 (6.35)
Sex (female)	2 females	3 females	4 females
Education (years)	10.46 (3.59)	12.00 (2.10)	11.94 (2.30)
IQ	91.84 (19.15)	88.00 (21.12)	94.58 (11.46)
Duration of illness (years)	12.30 (4.13)	13.30 (4.32)	–
mg equivalents Chlorpromazine/day	253.07 (165.59)	321.80 (248.49)	–
SANS (%)	59.33 (22.54)	27.45 (7.89)	–
SAPS (%)	16.77 (9.25)	51.87 (10.39)	–
Dual Task RT			
ST	585 (106)	478 (112)	378 (71)
DT	950 (167)	676 (124)	502 (145)
Dual-task cost	365 (172)	198 (94)	124 (100)

Means and standard deviations (in parenthesis) are reported.
 SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; RT = Reaction Time;
 ST = Single Task Condition; DT = Dual Task Condition.

abuse, of major affective or schizoaffective disorder, or a history of head injury or neurological damage or a childhood developmental disorder were excluded from the study. None of the controls showed either personal or family history of psychopathology. All subjects with schizophrenia were outpatients of the Psychiatry Department of Teramo at the time of testing and had a duration of illness between 5 and 23 years.

On the day of testing, the current symptomatology of the schizophrenic subjects was assessed by two psychiatrists using the Scale for the Assessment of Negative Symptoms (SANS) (25) and the Scale for the Assessment of Positive Symptoms (SAPS) (26).

The schizophrenic sample was divided into two subgroups: negative versus positive symptoms.

All the schizophrenic subjects, with the exception of two positive schizophrenics, were also administered three neuropsychological tests for assessment of executive functions: the WCST (27), the Tower of London Test (TLT) (28), and a Phonemic Verbal Fluency Test (PVFT) (29). The WCST (128 cards) was administered with standard instructions, as described by Spreen and Strauss (30), whereas scoring followed Heaton's (27) rules. The dependent variables were number of categories correctly achieved and number of perseverative errors (**Table 2**). Scoring and administration instructions for the TLT were those described by Krikorian et al. (31). Scoring and administration instructions of the PVFT were those described by Novelli et al. (29).

Stimuli and procedure

Subjects sat in front of a CRT screen driven by an Epson computer. The room where the experiments took place was in half-light. The middle of the computer screen was aligned with the subject's midline. The approximate distance of the eyes from the screen was 57 cm. The stimuli (1.5° x 5.5°) were placed 10° to the left or right of a central fixation point (1° x 1°). Each stimulus comprised two letters vertically placed one above the other, which were either the same or different.

The stimuli appeared according to a quasi-random sequence, with the constraints that there were an equal number of left and right side presentations and an equal number of same and different stimuli. Every trial began with the central fixation point, which stayed on the screen for 300 msec, followed by a 500 msec blank and by the onset of the stimuli, presented for 2 sec, and by an inter stimulus interval of 2 sec.

Every subject performed in two conditions (Single and Dual-task) of 72 trials each. The Single-Task condition (ST) required responding to the position (right or left) of the stimuli, pressing as rapidly as possible one of two keys of the computer keyboard. The stimulus-response mapping was compatible: the left stimuli required a response with the left key and right stimuli required a response with the right key. RT was recorded. The Dual-Task (DT) condition required to make a response to the position of the stimuli (as in the ST condition), then to say aloud whether the two letters were the same or different (no RT was

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Table 2. Neuropsychological results for the Negative and Positive Schizophrenics in Experiment 1

Measure	Schizophrenic subjects		t	P
	Negatives (n = 13)	Positives (n = 8)		
WCST	3.84 (2.07)	3.37 (1.84)	t (19)=.526	.605
No. of categories				
WCST	16.38 (14.86)	21.50 (12.78)	t (19)=-.805	.431
No. of perseverative errors				
Tower of London Test	23.84 (7.09)	19.87 (6.35)	t (19)=1.294	.211
Phonemic Verbal Fluency Test	5.38 (3.48)	4.08 (2.63)	t (19)=-.903	.378

Control subjects: WCST number of categories: 4.8±1.6; WCST number of perseverative errors: 11.3±8.7; Tower of London Test: 33.2±2.1; Phonemic Verbal Fluency Test: 37.26±8.08.

Means, standard deviations (in parenthesis), t and p values are reported.
WCST = Wisconsin Card Sorting Test.

recorder for the verbal secondary task). The two tasks had not to be executed at the same time, but rather in sequence (first the manual left-right discrimination task and then the verbal same-different discrimination task).

The instructions stressed the importance of speed in pressing the correct key in the left-right discrimination, but also placed some emphasis on the accuracy for both the left-right and the same-different discriminations. It is important to note that in the DT condition there was no time pressure for verbal response, because an interval of 2 sec elapsed between the manual response and the beginning of the following trial. When an error occurred, in the left-right discrimination task, then the stimulus was represented at the end of the block of trials.

All the subjects started with the ST condition and then performed the DT condition. Both conditions were preceded by some practice trials. The experimental trials were divided into two blocks of 36 trials each, between which the subjects were allowed to take a brief rest.

Experiment 2: The Simon task

In the Simon task, the relevant stimulus dimension, to which the subject has to respond pressing a key on the keyboard, is a non-spatial physical feature, like shape. In contrast, the location (left or right) in which the stimulus occurs is irrelevant. The Simon effect refers to the fact that responses are faster when the stimulus location corresponds to the location of the assigned response (corresponding trials) than when it does not (non-corresponding trials).

Because there is evidence that the Simon effect originates as a consequence of attention orienting toward the stimulus that appears to the left or right of fixation (32,33) the aim of this experiment was to assess orienting of attention (i.e., the posterior attention system) in negative and positive schizophrenics and in controls. To our knowledge only, a study of Gastaldo et al. (11) used the Simon task

with schizophrenic patients, but that study examined only patients with negative symptomatology.

Subjects

Twenty-five patients and the same 17 normal controls of Experiment 1 participated in Experiment 2. Fifteen schizophrenics (ten negative and five positive) participated also in Experiment 1. Ten new patients (four with negative and six with positive symptomatology) were also examined (Table 3).

Stimuli and procedure

The stimuli were white filled squares (with a side of 0.5°) or white filled circles (with a diameter of 0.5°), presented about 7.5° to the left or the right of the central fixation cross (1° x 1°).

The instructions were to press the response button corresponding to the particular stimulus figure as soon as it appeared on the screen. Response buttons were placed one on the left side and one on the right side of the computer keyboard. Half of the participants were asked to respond with the right hand to the square and with the left hand to the circle, regardless of the side in which the stimulus appeared. The other half of the participants were asked to respond with the right hand to the circle and with the left hand to the square, regardless of the side in which the stimulus appeared. Also, the participant was instructed to keep fixation at the centre and to respond as fast as possible. The stimulus stayed on the screen for 2 sec or until response execution. After the response, the screen remained empty for 500 msec, and then the subsequent trial was presented.

Subjects received a practice session of 60 stimuli and an experimental session of 240 stimuli.

The experimental trials were divided into four blocks of 60 trials each, between which the subjects were given a feedback on the mean correct RTs. Incorrect trials were not presented again and RTs slower than 2 sec were con-

Table 3. Experiment 2: Demographic, clinical details and results in the Simon task for the three groups (Negative and Positive Schizophrenics and Controls)

	Schizophrenic subjects		Controls n=17
	Negatives n=14	Positives n=11	
Age (years)	31.78 (4.59)	33.27 (5.58)	30.82 (6.35)
Sex (Female)	3 females	3 females	4 females
Education (years)	11.35 (3.41)	12.54 (1.50)	11.94 (2.30)
IQ	91.35 (18.73)	90.36 (12.33)	94.58 (11.46)
Duration of illness (years)	11.50 (4.39)	13.36 (3.72)	-
Mg equivalents Chlorpromazine/day	206.42 (161.98)	149.81 (126.44)	-
SANS (%)	65.85 (19.53)	19.40 (13.84)	-
SAPS (%)	15.34 (9.82)	45.38 (23.68)	-
Simon task RT			
Corresponding trials	644 (114)	589 (74)	524 (75)
Non-corresponding trials	644 (108)	642 (75)	550 (76)
Simon effect	-.29 (29)	53 (31)	26 (26)

Means and standard deviations (in parenthesis) are reported.
SANS = Scale for the Assessment of Negative Symptoms; SAPS = Scale for the Assessment of Positive Symptoms; RT = Reaction Time.

sidered to be omissions. In each session, half of the stimuli were squares and half were circles. Half the time the stimulus was shown in the right visual hemifield and half in the left. The sequence was randomized, producing the following conditions:

50% of corresponding trials, in which the correct response and the stimulus were on the same side (right-right and left-left);

50% of non-corresponding trials, in which the side of the correct response did not coincide with the side of stimulus presentation (i.e., right-left and left-right).

RESULTS

Experiment 1

Clinical and neuropsychological scale

The current intellectual functioning of each subject was assessed using the Raven test. Thirteen schizophrenics resulted to have prevalent negative symptomatology and 10 schizophrenics resulted to have prevalent positive symptomatology. The mean global rating on the SANS for the negative symptom group was significantly higher in comparison to the positive symptom group ($t(21)=4.25, p<.0001$). The mean global rating on the SAPS scale in the positive-symptom group was significantly higher in comparison with the

negative symptom group ($t(21)=-8.55, p<.0001$). Positive and negative schizophrenics did not show any difference in age ($t(21)=-.769, p=.450$), years of education ($t(21)=-1.20, p=.244$), IQ ($t(21)=.457, p=.653$), duration of illness ($t(21)=-.560, p=.581$) and mean daily chlorpromazine equivalent dose ($t(21)=-.796, p=.435$). Moreover, schizophrenics and controls did not show any difference in age [$t(28)=.751, p=.459$ for negative, and $t(25)=1.30, p=.204$ for positive schizophrenics], years of education [$t(28)=-1.37, p=.181$ for negative, and $t(25)=.066, p=.984$ for positive schizophrenics] and IQ [$t(28)=-.488, p=.629$ for negative, and $t(25)=-1.05, p=.301$ for positive schizophrenics].

In the neuropsychological assessment, the Z score of each test was calculated to measure how much the schizophrenic groups diverged from the mean of a normative sample. Deficits were evident for both groups (negative and positive schizophrenics) in the TLT (-4.45 and -6.34, respectively) and in the PVFT (-3.94 and -4.10, respectively), whereas performance in the WCST was close to the normative sample.

The raw scores of the neuropsychological tests were entered into multiple two-tailed t-tests. No differences between negative and positive schizophrenics were significant (Table 2).

Data analyses

Analyses of variance (ANOVAs) were carried out on absolute and proportional correct RTs. The ab-

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solute RT analyses refer to absolute differences in RT induced by the experimental manipulations. The proportional RT analyses were carried out to control for the different baseline of patients and controls. It often happens that slower subjects benefit more from factors that speed up RT and suffer more from factors that slow down RT, than subjects with faster baseline RTs. Given that patient groups in general, and, as will be shown, also in this study, are markedly slower than controls in baseline conditions, it seemed safer to run also the proportional analyses. Therefore, we estimated for each subject the proportional dual-task cost as (dual-task RT/single-task RT). A covariate analysis taking into account QI, age and years of education was also carried out.

For all the analyses reported in the paper, the significance level chosen was .05 and the post-hoc comparisons were performed with the Student-t-test method. Moreover, the results on proportional data and on covariate analyses were reported in details only when they did not replicate the results of the analyses on absolute RTs.

Mean correct RTs for the left-right discrimination were entered into an ANOVA. The between-subjects factor was group (normal controls, negative and positive schizophrenics); the within-subjects factors were task (ST or DT) and side of presentation (left or right). The proportional RT dual-task costs were submitted to an ANOVA with Group as the between-subjects factor.

The factor group was significant, ($F=34.58$; $df=2.37$; $p<.0001$) as was the factor Task ($F=125.46$; $df=1.37$; $p<.0001$). Schizophrenics with negative and positive symptoms showed longer RTs than controls (767, 577, and 440 msec, respectively). Moreover, schizophrenics with negative symptoms showed significantly longer RTs than schizophrenics with positive symptoms. The DT condition was 229 msec slower than the ST condition (709 vs. 480 msec).

The most interesting interaction for the purpose of this study (group x task) was highly significant ($F=13.56$; $df=2.37$; $p<.0001$). Post-hoc tests showed that the dual-task cost (DT condition minus ST condition) was significantly greater for the negative schizophrenics than for positive schizophrenics ($p<.01$) and controls ($p<.0001$) (**Table 1**). The difference between positive schizophrenics and controls did not reach significance ($p=.468$).

The proportional dual task analysis replicated the main results, being of 1.65, 1.44, and 1.31, for negative, positive schizophrenics and controls ($F=5.52$; $df=2.37$; $p=.008$). Again, the dual-task cost was significantly greater for the negative schizophrenics than for controls ($p=.006$).

A covariate analysis taking into account QI, age and years of education replicated these results.

Experiment 2

Clinical scale

The mean global rating on the SANS for the negative symptom group was significantly higher in comparison to the positive symptom group ($t(23)=6.66$, $p<.0001$). The mean global rating on the SAPS scale in the positive-symptom group was significantly higher in comparison with the negative symptom group ($t(23)=-4.31$, $p<.0001$). Positive and negative schizophrenics did not show any difference in age [$t(23)=-.731$, $p=.472$], years of education [$t(23)=-1.072$, $p=.295$], IQ [$t(23)=.152$, $p=.881$], duration of illness [$t(23)=-1.123$, $p=.273$] or mean daily chlorpromazine equivalent dose [$t(23)=.952$, $p=.351$]. Schizophrenics and controls did not show any difference in age [$t(29)=.473$, $p=.640$ for negative, and $t(26)=1.04$, $p=.307$ for positive schizophrenics], years of education [$t(29)=-.567$, $p=.575$ for negative, and $t(26)=.767$, $p=.450$ for positive schizophrenics] and IQ [$t(29)=-.590$, $p=.560$ for negative, and $t(26)=-.925$, $p=.364$ for positive schizophrenics].

Data analyses

ANOVAs were carried out on absolute and proportional correct RTs. Therefore, we estimated for each subject the proportional Simon effect as (non-corresponding trials/corresponding trials). A covariate analysis taking into account QI, age and years of education was also carried out. The results on proportional data and on covariate analyses were reported in details only when they did not replicate the results of the analyses on absolute RTs.

Mean correct RTs were entered into an ANOVA. The between-subjects factor was group (normal controls, negative and positive schizophrenics); the within-subjects factor was spatial correspondence (corresponding vs. non-corresponding trials). Group ($F=6.21$; $df=2.39$; $p<.005$) and spatial correspondence ($F=33.44$; $df=1.39$; $p<.0001$) were significant. RTs of schizophrenics with negative and positive symptoms and controls were 644, 615, and 537 msec, respectively. Schizophrenics with negative symptoms showed significantly longer RTs than controls. Non-corresponding trials were 26 msec slower than corresponding trials (612 vs. 586 msec).

The most interesting interaction for the purpose of this study (group x spatial correspondence interaction) was highly significant ($F=10.64$; $df=2.39$; $p<.0001$) too.

Post-hoc tests showed that the Simon effect (non-corresponding trials minus corresponding trials) was significant for controls ($p < .001$) and positive schizophrenics ($p < .0001$), whereas it was absent for negative schizophrenics ($p = .969$) (**Table 3**).

Negative and positive schizophrenics were significantly slower than controls in both corresponding and non-corresponding trials ($p < .001$ and $p = .008$ respectively for negative schizophrenics; $p = .033$ and $p = .004$, respectively for positive schizophrenics). Negative schizophrenics were not significantly slower than positive schizophrenics in either corresponding or non-corresponding trials ($p = .180$, $p = .959$, respectively).

Interestingly, negative schizophrenics showed a significantly smaller Simon effect than controls ($p = .016$), whereas positive schizophrenics showed a significantly greater Simon effect than controls ($p = .018$).

The proportional analysis replicated the main results, the Simon effect being of 1.00, 1.09, and 1.05, for negative, positive schizophrenics and controls ($F = 8.75$; $df = 2.39$; $p < .001$).

A covariate analysis taking into account QI, age and years of education replicated these results.

DISCUSSIONS

The anterior and posterior attention systems in schizophrenic patients were examined through two experiments: a dual-task paradigm evaluates executive functions, with specific regard to planning and coordination and a Simon task evaluates automatic shifting of visual attention. The dual-task paradigm replicated what previously found with normal subjects (20). The speeded left-right discrimination took longer when subjects were also instructed to perform the unspeeded same-different discrimination. Umiltà et al. (20) demonstrated that the locational discrimination was not delayed because of the presence of the secondary task, but rather because location and shape information are available at the same time. The extra time needed to perform the primary task in the presence of the secondary task is due to the coordination of the two tasks. The coordination of the two tasks was required because subjects had to decide which response to emit first, that is the one concerning location or the one concerning shape. Schizophrenics were significantly slower than controls. Moreover, schizophrenics with negative symptoms were significantly slower than schizophrenics with positive symptoms. Even more interestingly, the dual-task cost was significantly greater for negative schizophrenics than for positive schizophrenics and controls. Apparently, when negative schizophrenics had to perform two tasks they took longer in

planning the sequence of the two responses. That suggests that negative schizophrenics have a deficit that affects the functioning of the SAS, which is called upon in planning and decision-making. The ability to co-ordinate two actions is significantly better in positive schizophrenics. This result is particularly interesting also considering that negative and positive schizophrenics did not show any difference in age, education, IQ, duration of illness or mg equivalent Chlorpromazine dose for day. The dual-task performance of negative schizophrenics resembled what previously found in CHI patients and anterior communicating artery aneurysm patients (34-36). The neuropsychological examination showed deficits for executive functions, especially when examined with the TLT and the PVFT. Surprisingly, no differences between negative and positive schizophrenics were significant. It seems that the dual-task paradigm has a greater sensitivity to detect differences in executive functions between negative and positive schizophrenics. The Simon effect is likely to originate because attention is oriented to the target stimulus and this produces the spatial code of the stimulus, even through this code is task irrelevant (32,33). The spatial code of the stimulus in turn activates the corresponding response, that is the response that shares the same spatial code as the stimulus. When the automatically activated corresponding response is not the one required by the task, it must be inhibited, causing a delay in responding. When it is the one required by the task, facilitation is observed.

Here we found that only negative schizophrenics lacked the Simon effect and the reason for that was that the congruent condition was much slow. Thus, it seems that negative schizophrenics are able to inhibit an automatically activated but incorrect response, whereas they are not able to benefit from an automatically activated correct response. An alternative possibility is that they have a deficit in the posterior attentional system and cannot orient attention to the target stimulus. Because of that the stimulus spatial code is not formed, the corresponding response is not activated, and, therefore, the congruent and incongruent conditions are equivalent. In addition, the failure to orient attention to the stimulus renders responses overall slower. In a previous paper (11), in which different negative schizophrenics were tested with the Simon task, a similar lack of the Simon effect was found, but it was confined to the left visual field.

Interestingly, the Simon effect was significantly greater for positive schizophrenics (52 ± 30) than for controls (26 ± 26). Thus, it seems that positive schizophrenics are slower than controls in inhibiting an automatically activated but incorrect response.

CONCLUSIONS

Experiment 1 has shown that negative schizophrenics are impaired in performing a dual-task which depends on the anterior attention system. That is consistent with the notion that schizophrenics are impaired in executive functions, and negatives are more severely impaired than positives. This result can be generally described as confirming the syndrome presented by schizophrenic patients (9). In effect, executive deficits are viewed as a clear impairment in the ability of engaging in motivated and purposeful behaviour, even when positive symptoms are absent or have been already treated.

Since the description in schizophrenia of key deficits in attention, perception and cognition by early psychopathologists (18,33,37), experimental psychopathologists have tried to identify the core abnormalities of information processing. A controversy about cognition in schizophrenia was whether schizophrenics performed equally poorly in every test, producing a global intellectual deficit or had greater deficits in one or more aspects (38,39). This controversy is still ongoing, with some researchers believing that the main cognitive deficit in schizophrenia is a massive impairment in all skill areas, whereas others believe that specific deficits exist in definite areas, such as memory and attention, besides an overall poor performance (40).

Our results support the idea that specific symptom dimensions or patterns are associated to specific cognitive impairments. What is particularly striking is that negative schizophrenics manifested clear abnormalities, whereas positive schizophrenics performed very similarly to healthy controls. In effect, in the first experiment only negative schizophrenics showed a pronounced deficit in coordinating two tasks. That is consistent with well-documented observations stating that patients with schizophrenia are impaired in performing divided attention tasks (4,41,42).

The results of the second experiment are consistent with observations of association between distractibility and disorganization symptoms and poor selective attention (40). Disorganization symptoms have even been made into an independent dimension of the illness, the so-called "disorganization" syndrome (39, 43). However, also in this experiment, the abnormality that can be attributed to a deficit in attention orienting, that is the absence of the Simon effect, is limited to the negative schizophrenics. A possible link between attention deficits and negative symptoms derives from the suggestion that the pattern of deficits in attentional functioning in schizophrenic patients and groups at risk for schizophrenia is consistent with a reduction in available processing capacity (44,45).

It is of interest that recent studies claim that different neuropsychological deficits underlie different symptoms, with different neurophysiological substrates (16,17). Brain imaging evidence of activation of different brain areas in response to complex neuropsychological testing is reported (46). In a previous contribution, we have highlighted the strong relation between neurocognitive deficits, social cognition deficits and negative symptoms (47).

Schizophrenia has been related to a prefrontal dysfunction (18,48,49). Sereno and Holtzman (50) showed that in schizophrenic subjects there is a deficit in voluntary attentional control, with disinhibition and therefore enhancement of automatic processes of spatial selective attention. From these considerations, cognitive impairment in schizophrenia and more specifically attentional impairment would be linked to hypofrontality and the predominance of negative symptoms.

In any case, cognitive impairment tends to be relatively independent of the symptoms of the illness. In general terms, negative symptoms tend to be more strongly correlated with cognitive performance than positive symptoms. The former may covary with measures of executive function and visual-motor performance; the latter tend to correlate with measure of auditory distractibility and other forms of auditory processing (10,18). There is agreement among researchers that the symptoms of schizophrenia do not "cause" cognitive impairment; instead these two domains appear to reflect different aspects of the underlying neurobiology of the disease. In particular, attentional impairments appear to persist after remission of acute psychotic episodes and occur over the entire course of the illness. Moreover, multiple attention deficits have been observed in individuals with schizotypal disorder and children of schizophrenics (40), thus supporting the view of attention deficits as an early marker of the illness.

REFERENCES

1. Berrios GE. Positive and negative signals: a conceptual history. In: Marnero SA, Andreasen NC, Tsuang MT (eds). *Negative Versus Positive Schizophrenia*. Berlin, Germany: Springer-Verlag Berlin; 1991: 8-27.
2. Crow TJ. Molecular pathology of schizophrenia: more than one disease process? *Br Med J* 1980; 280: 66-8 .
3. Andreasen NC, Olsen S. Negative versus positive schizophrenia. *Arch Gen Psychiatry* 1982; 39: 789-94.
4. Notebaert W, Soetens E, Melis A. Sequential analysis of a Simon task: evidence for an attention-shift account. *Psychol Res* 2001; 65: 170-84.
5. Strauss JS, Carpenter WT Jr, Bartko JJ. An approach to the diagnosis and understanding of schizophrenia: Part III. Speculations on the processes that underlie schizophrenic symptoms. *Schizophr Bull* 1974; 1 (Experimental Issue No. 11): 61-70.

6. Crow TJ. Schizophrenic deterioration: discussion, 3. *Br J Psychiatry* 1983; 143: 80-1.
7. Nuechterlein KH. Vigilance in schizophrenia and related disorders. In: Steinhauer SR, Gruzelier JH, Zubin J (eds). *Handbook of Schizophrenia*. Vol. 5. Neuropsychology, Psychophysiology, and Information Processing. New York: Elsevier, 1991.
8. Buchanan RW, Strauss ME, Kirpatrick B, Holstein C, Breier A, Carpenter WT Jr. Neuropsychological impairments in deficits vs. Nondeficit forms of schizophrenia. *Arch Gen Psychiatry* 1994; 51: 804-11.
9. Reilly JL, Harris MSH, Khine TT, Keshavan MS, Sweeney JA. Reduced attentional engagement contributes to deficits in prefrontal inhibitory control in schizophrenia. *Biol Psychiatry* 2008; 63: 776-83.
10. Strauss ME, Buchanan RW, Hale J. Relations between attentional deficits and clinical symptoms in schizophrenic outpatients. *Psychiatry Res* 1993; 47: 205-13.
11. Gastaldo S, Umiltà C, Bianchin G, Prior M. The Simon effect in schizophrenic patients with negative symptoms. *Cortex* 2002; 38: 149-59.
12. Lopes-Machado E, Crippa JA, Hallak JEC, Guimaraes FS, Zuardi AW. Electrodermally nonresponsive schizophrenia patients make more errors in the Stroop Color Word Test, indicating selective attention deficit. *Schizophr Bull* 2002; 28: 459-66.
13. Williams LM. Cognitive inhibition and schizophrenic symptom subgroups. *Schizophr Bull* 1996; 22: 139-51.
14. Park S, Pueschel J, Sauter BH, Rentsch M, Hell D. Spatial selective attention and inhibition in schizophrenia patients during acute psychosis and at 4-month follow-up. *Biol Psychiatry* 2002; 51: 498-506.
15. Posner MI, Dehaene S. Attentional networks. *Trends in Neuroscience* 1994; 17: 75-9.
16. Norman RMG, Malla AK, Morrison-Stewart SL, et al. Neuropsychological correlates of syndromes in schizophrenia. *Br J Psychiatry* 1997; 170: 134-9.
17. Guillem F, Bicu M, Bloom D, et al. Neuropsychological impairments in the syndromes of schizophrenia: a comparison between different dimensional models. *Brain Cogn* 2001; 46: 153-9.
18. Carter JD, Bizzell J, Kim C, Bellion C, Carpenter KLH, Dichter G, Belger A. Attention deficits in schizophrenia: preliminary evidence of dissociable transient and sustained deficits. *Schizophr Res* 2010; 122: 104-12.
19. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. Washington, DC: American Psychiatric Press, 1994.
20. Umiltà C, Nicoletti R, Simion F, Tagliabue ME, Bagnara S. The cost of a strategy. *European Journal of Cognitive Psychology* 1992; 4: 21-40.
21. Pashler H, Johnston JC. Chronometric evidence for central postponement in temporally overlapping tasks. *Q J Exp Psychol A* 1989; 41: 19-45.
22. Pashler H. Dual-task interference in simple tasks: data and theory. *Psychol Bull* 1994; 116: 220-44.
23. Shallice T. *From neuropsychology to mental structure*. Cambridge: Cambridge University Press, 1988.
24. Shallice T. Multiple levels of control processes. In: Umiltà C, Moscovitch C (eds). *Attention and performance XV: conscious and nonconscious information processing*. Cambridge, Mass.: MIT Press, 1994.
25. Andreasen NC. *Scale for the Assessment of Negative Symptoms (SANS)*. Iowa City: University of Iowa, 1981.
26. Andreasen NC. *Scale for the Assessment of Positive Symptoms (SAPS)*. Iowa City: University of Iowa, 1983.
27. Heaton RK. *Wisconsin Card Sorting Test Manual*. Odessa, FL: Psychological Assessment Resource, 1981.
28. Shallice T. Specific impairments of planning. *Philos Trans R Soc Lond B Biol Sci* 1982; 298: 199-209.
29. Novelli G, Papagno C, Capitani E, Laiacona M, Vallar G, Cappa SF. Three clinical tests for the assessment of lexical retrieval and production. Norms from 320 normal subjects. *Arch Psicol Neurol Psychiatr* 1986; 47: 477-506.
30. Spreen O, Strauss E. *A compendium of neuropsychological tests: administration, norms, and commentary*, II ed. London: Oxford University Press, 1998.
31. Krikorian R, Bartok J, Gay N. Tower of London procedure: a standard method and developmental data. *J Clin Exp Neuropsychol* 1994; 16: 840-50.
32. Nicoletti R, Umiltà C. Attention shifts produce spatial stimulus codes. *Psychol Res* 1994; 56: 144-50.
33. Rubichi S, Nicoletti R, Iani C, Umiltà C. The Simon effect occurs relative to the direction of an attention shift. *J Exp Psychol Hum Percept Perform* 1997; 23: 1353-64.
34. Stablum F, Umiltà C, Mogentale C, Carlan M, Guerrini C. Rehabilitation of executive deficits in closed head injury and anterior communicating artery aneurysm patients. *Psychol Res* 2000; 63: 265-78.
35. Stablum F, Leonardi G, Mazzoldi M, Umiltà C, Morra S. Attention and control deficits following closed head injury. *Cortex* 1994; 30: 603-18.
36. Stablum F, Mogentale C, Umiltà C. Executive functioning after mild closed head injury. *Cortex* 1996; 32: 261-78.
37. Braff DL, Light GA. Preattentive and attentional cognitive deficits as targets for treating schizophrenia. *Psychopharmacology* 2004; 174: 75-85.
38. Chapman JP, Chapman LJ. Reliability and the discrimination of normal and pathological groups. *J Nerv Ment Dis* 1983; 171: 658-61.
39. Luck SJ, Gold JM. The construct of attention in schizophrenia. *Biol Psychiatry* 2008; 64: 34-9.
40. Harvey PD, Sharma T. *Understanding and treating cognition in schizophrenia: a clinician's handbook*. London: Martin Dunitz, 2002.
41. Serper MR, Bergman RL, Harvey PD. Medication may be required for the development of automatic information processing in schizophrenia. *Psychiatry Res* 1990; 32: 281-8.
42. Granholm E, Asarnow RF, Marder SR. Controlled information resources and the development of automatic detection responses in schizophrenia. *J Abnorm Psychol* 1991; 100: 22-30.
43. H_schel K, Irle E, Rütger E. Psychopathological symptoms and test performance in schizophrenic patients. *Fortschr Neurol Psychiatr* 1998; 66: 512-9.
44. Nuechterlein KH, Dawson ME. Information processing and attentional functioning in the developmental course of schizophrenic disorders. *Schizophr Bull* 1984; 10: 160-203.
45. Gouzoulis-Mayfrank E, Balke M, Hajsamou S, et al. Orienting of attention in unmedicated patients with schizophrenia, prodromal subjects and healthy relatives. *Schizophr Res* 2007; 97: 35-42.
46. Bullmore E, Fletcher P. The eye's mind: brain mapping and psychiatry. *Br J Psychiatry* 2003; 182: 381-4.
47. Mazza M, De Risio A, Surian L, Roncone R, Casacchia M. Selective impairments of theory of mind in people with schizophrenia. *Schizophr Res* 2001; 47: 299-308.
48. Levin S. Frontal lobe dysfunctions in schizophrenia -II: impairments of psychological and brain functions. *J Psychiatr Res* 1984; 18: 57-72.
49. Fuller RL, Luck SJ, Braun EL, Robinson B, McMahon RP, Gold JM. Impaired control of visual attention in schizophrenia. *J Abnorm Psychol* 2006; 115: 266-75.
50. Sereno AB, Holzman PS. Spatial selective attention in schizophrenic, affective disorder, and normal subjects. *Schizophr Res* 1996; 20: 33-50.