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'Hyper-priming' in thought-disordered schizophrenic patients

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ABSTRACT

Background. A number of studies have suggested that indirect semantic priming is enhanced in thought-disordered schizophrenics. However, research on direct semantic priming has produced conflicting results. The aim of the present study was to resolve some of the ambiguities of previous findings.

Methods. For the present study, 44 schizophrenic patients were split according to the presence of associative loosening into a positive thought-disordered (TD) and non-positive thought-disordered (NTD) group. Thirty healthy subjects and 36 psychiatric patients served as controls.

Results. Schizophrenics displayed increased indirect semantic priming compared with psychiatric controls. When subtyping the sample, TD-patients exhibited significantly enhanced indirect semantic priming compared with healthy and psychiatric controls as well as NTD-patients. Overall slowing was found to be independent of priming effects. Medication, age and chronicity of the schizophrenic illness did not modulate priming.

Conclusions. In line with Spitzer and Maher it is inferred that disinhibited semantic networks underlie formal thought disorder in schizophrenia. For future research, it would be appropriate to: employ indirect semantic priming rather than direct semantic priming conditions; and, pay more attention to potential moderators of the priming effect, most importantly, the prime display duration and the length of the stimulus onset asynchrony.

INTRODUCTION

Language disturbances are among the most prominent psychopathological features of schizophrenia. Beyond the acute psychotic phase, many schizophrenic patients exhibit language dysfunctions such as loosening of associations, clanging, and tangential speech.

Using the experimental arsenal of cognitive psychology, much research has been devoted to shedding light on processes putatively underlying thought and language dysfunctions in schizophrenia (Spitzer, 1997; Aloia *et al*. 1998). Starting with Maher and Manschreck (Maher *et al*. 1987; Manschreck *et al*. 1988), many researchers have employed the semantic priming technique to study the semantic architecture and the dynamic stream of associations in schizophrenia (Weisbrod *et al*. 1998). Semantic priming procedures allow us to estimate how far and how fast associations run through the semantic network. In such tasks, two stimuli (the first stimulus is usually referred to as the prime; the second is called the probe) are successively presented. Whereas the prime has to be simply attended to without overt response in most experiments, the subject is instructed either to name the second stimulus (word pronunciation procedure) or to decide whether the probe is either a string of meaningless characters or a meaningful word (lexical decision procedure). A semantic priming effect is reliably obtained when a target word (e.g. sister) is preceded by a semantically or contextually related word (e.g.

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brother), relatedness is usually derived from association norm studies. Reaction times (RTs) are faster and the accuracy of decision is higher as compared to a trial in which unrelated words (e.g. door – apple) are successively presented (Meyer & Schvanefeldt, 1971; Neely, 1977, 1991). According to cognitive psychology, this effect is often attributed to spreading activation from the prime to the target word, which induces a lowered activation threshold for the probe stimulus (Collins & Loftus, 1975).

Maher and Manschreck (Maher *et al*. 1987; Manschreck *et al*. 1988) inferred that heightened or longer-lasting spread of activation serves as a major contributor to formal thought disorder, i.e. that associations in thought-disordered patients spread faster than in normal subjects. In line with their initial hypothesis, using a lexical decision design they demonstrated that thought-disordered schizophrenic patients (TD) exhibit larger semantic priming effects than healthy and depressive controls.

However, the literature on semantic priming in schizophrenia has remained largely inconsistent. Although the basic findings of Maher, Manschreck and colleagues have been confirmed in several studies conducted with American (Kwapil *et al*. 1990) and German patient samples (Baving, 1998; Spitzer *et al*. 1993*a*, *b*; Weisbrod *et al*. 1998), other researchers have found either an attenuation of semantic priming in thought-disordered schizophrenics or no substantial differences between both groups (e.g. Henik *et al*. 1992; Vinogradov *et al*. 1992; Passerieux *et al*. 1995, 1997). In view of these conflicting findings, several potential moderators of the semantic priming effect need thorough consideration, as follows.

Length of illness

Maher *et al*. (1996) reported that the amount of semantic priming is inversely correlated with the duration of the schizophrenic illness, i.e. subjects with a chronic history of schizophrenia have been found to exhibit attentuated semantic priming while recent-onset schizophrenic patients show enhanced priming. Therefore, Maher *et al*. (1996) account for the failure of Vinogradov *et al*. (1992) and others to replicate their results by the chronicity of the patients investigated.

Stimulus onset asynchrony

A large body of research from cognitive psychology suggests that a stimulus onset asynchrony (SOA; i.e. the interval between prime and probe onset) below 500 ms taps automatic spreading of activation (Posner & Snyder, 1975; Neely, 1977, 1991). SOAs above 500 ms are likely to be affected by controlled/conscious processes such as expectancy (expectancy effects may play a role even at an SOA of 400 ms; Vinogradov *et al*. 1992) and semantic matching (semantic matching, however, does only work in lexical decision tasks whereas expectancy has been reported in both word pronunciation and lexical decision tasks; Neely, 1991).

Unfortunately, many studies have employed SOAs above (Aloia *et al*. 1998) or at the border (Kwapil *et al*. 1990; Besche *et al*. 1997; Passerieux *et al*. 1997) of these divergent processing modes. However, a relative attention of semantic priming in schizophrenics for SOAs beyond 500 ms does not challenge the initial hypothesis of Manschreck and Maher (Maher *et al*. 1987) as it is undisputed that schizophrenic patients show disturbed working memory (as a result, healthy subjects are able to raise their priming effects to a comparatively larger degree than schizophrenics when longer SOAs are used allowing for more deliberate processing). According to Maher *et al*. (1987) the core deficit has to be inferred for the automatic processing mode.

Critical stimulus duration

It is empirically well established that schizophrenic patients need longer critical stimulus durations, i.e. that schizophrenics need longer display times to perceive verbal or other material (see for example Cadenhead *et al*. 1997). Since several studies have employed tasks in which prime words were presented below 100 ms (at 50 ms, Ober *et al*. 1995; Vinogradov *et al*. 1992 and at 60 ms, Ober *et al*. 1997), future research should address the hypothesis that semantic priming was simply diminished due to perceptual processing deficits in these patients.

Medication

Several studies converge in the assumption that semantic priming is: modulated by the dopamine

system (for a review see Spitzer, 1997); and, is sensitive to the effects of psilocybin (Spitzer *et al*. 1996). Therefore, investigations reporting larger priming effects in TD schizophrenics may have been biased by the fact that TD patients usually receive higher doses of neuroleptics (see for example, Maher *et al*. 1987), which have been shown to enhance priming in some studies (Barch *et al*. 1996). Therefore, when demonstrating larger priming-effects in TD as compared to NTD patients, the possibility of these effects being linked to different medication baselines has to be investigated.

Computation of semantic priming

Although most semantic priming studies investigating 'special' groups (children, old people, schizophrenics, etc.) have expressed the semantic priming effect as a simple difference score, several arguments call for caution with concern to the adequacy of this approach. Chapman *et al*. (1994) laid down that semantic priming is likely to be inflated by the effects of prolonged reaction times (RTs) since enhanced RTs have been found to correlate with priming (see for example, Barch *et al*. 1996). They suggest that difference scores should be adjusted by the degree to which psychomotor slowing enhances semantic priming. Preferably, a large sample of healthy subjects should be used to evaluate the relationship, overall RTs are entered as the predictor variable for semantic priming in a linear regression analysis, the resulting raw regression coefficient is then entered into the equation to determine the adjusted difference score.

Definition of formal thought disorder

Thought disorder is not a unitary phenomenon (Vinogradov *et al*. 2000). Several factor analytical studies show that scores of rating scales such as the Thought, Language and Communication Scale (TLC) can be divided into several clearly distinguishable components (Peralta *et al*. 1992). Therefore, it is essential to specify the symptom(s) investigated. Formal thought disorder itself is an umbrella term with unsatisfactory explanatory power. Since previous studies employed different scales (BPRS-item 4, Overall & Gorham, 1988; TLC-global score, SADS (various symptoms), Spitzer & Endicott, 1977) for evaluating thought disorder, different aspects of formal thought disorder were presumably tapped.

Experimental condition (semantic/indirect semantic priming)

If it is assumed that schizophrenics do not only associate faster but also further, a superior method for evaluating the spread of activation would be to employ mediated word pairs (like chalk and black, both words are combined via an undisplayed mediator (white)), i.e. to employ conditions with a more remote associative relation. In a series of studies, Spitzer and colleagues (Spitzer *et al*. 1993*a*; Weisbrod *et al*. 1998) have demonstrated that schizophrenics, especially those with TD, exhibit enhanced indirect semantic priming for SOAs favouring automatic spreading activation.

To circumvent some of the problems aforementioned, we recently (Moritz *et al*. 1999) investigated 160 healthy subjects who were split according to the presence or absence of schizophrenia-like language disturbances (subscale 'language' of the Frankfurt Complaint Questionnaire, the items were derived from the verbal complaints of schizophrenic patients; Williams *et al*. 1984). As none of the subjects received psychotropic substances or revealed a history of mental illness, results could be directly interpreted in terms of automatic facilitation. In line with Spitzer (1997) and Maher *et al*. (1987), subjects showing higher degrees of schizophrenia-like language disturbances exhibited significantly enhanced direct and indirect semantic priming effects that were more pronounced for short SOA conditions. Importantly, both groups showed similar overall RTs.

The present study is the first investigation in which schizophrenic patients are compared with a psychiatric control group (patients either suffering from obsessive–compulsive disorder (OCD) or depression) with regard to indirect semantic priming. A major aim of this study was to evaluate whether (indirect) semantic priming effects are specific to schizophrenic psychopathology or whether other psychiatric groups show a similar pattern of results. To rule out some of the artefacts mentioned above, a semantic priming task was employed that used a short SOA (200 ms) and long prime display

times (200 ms, i.e. no interstimulus interval was employed). The effects of length of illness, age and medication were investigated by means of simple correlations. Moreover, before computing difference scores, regression data from a large healthy control group ($N = 160$) were inspected with regard to artificially inflated semantic priming effects as a possible consequence of prolonged reaction times.

METHOD

Subject

Psychiatric patients were recruited from the local university hospital: 44 schizophrenics, 36 psychiatric ($N = 17$ OCD patients, $N = 19$ depressive patients) and 30 healthy controls were investigated. All subjects were German. Each healthy participant was strictly matched to a schizophrenic patient with respect to gender, age (± 3 years) and years spent at school. All patients satisfied DSM-IV criteria. Diagnoses were made by experienced clinicians and further confirmed by means of a semi-structured interview (see below). Moreover, patients' files were screened for possible diseases incompatible with a diagnosis of schizophrenia. Subjects with a history of head injury and significant substance abuse did not participate. Sociodemographic and psychopathological variables are given in Table 1.

Most of the schizophrenic patients ($N = 35$) took part in a study evaluating the effects of atypical neuroleptics. At the time of testing, patients received different atypical agents (clozapine, risperidone, sertindole, zotepine or olanzapine) for at least 2 weeks following a wash-out period. No additional neuroleptic or anticholinergic agents were administered in these patients. Six patients did not take any neuroleptics for at least 2 weeks and three schizophrenic patients were treated with conventional neuroleptics.

The psychiatric control group was significantly older than both the schizophrenics and the healthy controls ($P \leqslant 0{\cdot}05$; the potential significance of this variable to predict semantic priming is analysed below). When the schizophrenic sample was split according to the presence of thought disorder, the age difference between the psychiatric controls and the non-thought-disordered group achieved significance. No other difference concerning sociodemographic variables (including length of illness) achieved significance (with regard to both the comparison of the controls with the entire schizophrenic sample and the schizophrenic subgroups). NTD and TD patients did not differ with respect to the dosage of neuroleptics administered (chlorpromazine equivalents were estimated according to Dietmaier & Laux, 1998: TD, 355·8 mg; NTD, 317·9 mg; $t = 0{\cdot}41$; $P > 0{\cdot}5$).

In order to split schizophrenic patients according to positive formal thought disorder, a newly developed rating scale the Positive and Negative and Disorganized Symptoms Scale was administered (PANADSS, Andresen & Moritz, 2000). The PANADSS is designed for rating major psychiatric symptoms on the basis of a semi-structured interview that takes approximately 45 min for each patient. Anchor points are provided for each degree of severity to raise inter-rater reliability (seven degrees for each symptom corresponding to the Positive and Negative Syndrome Scale (see Kay *et al*. 1989)). For many items, the formulation of the PANADSS anchor points closely resembles the definition of the PANSS items. However, several symptoms have been defined more thoroughly

Table 1. *Demographic characteristics of the samples* (*means and standard deviations*)

	Schizophrenic sample			Control sample	
	Entire group ($N = 44$)	NTD-group ($N = 28$)	TD-group ($N = 16$)	Healthy controls ($N = 30$)	Psychiatric controls ($N = 36$)
Age (years)	31·8 (10·3)	31·0 (9·7)	33·3 (11·5)	31·5 (9·4)	38·4 (10·6)
School education (years)	11·2 (1·8)	11·6 (1·8)	10·5 (1·8)	11·5 (1·5)	10·9 (1·5)
Gender (male/female)	28/16	17/11	11/5	20/10	16/20
Length of illness (years)	7·5 (8·3)	5·6 (6·9)	11·1 (9·9)	—	10·2 (9·3)
CPE (mg)	343·1 (277·0)	355·8 (314·5)	317·9 (188·7)	—	—

CPE, chlorpromazine equivalents; ND, non-thought-disordered schizophrenic subjects; TD, thought-disordered schizophrenic subjects.

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in the PANADSS and clinical examples are provided for most items. In contrast to the PANSS, different types of paranoid ideation, hallucinations and affect (especially flat and incongruent affect) are scored separately. The 'associative loosening' item of the PANADSS differs from the 'formal thought disorder' item of the PANSS in that the PANADSS item solely covers symptoms of derailed and loosened speech whereas the PANSS item assesses various abnormalities of speech, which probably reflect different pathologies (loosening of associations, thought blocking, mutism).

Factor analysis has confirmed the construct validity of the PANADSS since the three factor model of schizophrenia (positive, negative and disorganized symptomatology) was successfully replicated (Moritz *et al.* 2000). Ratings were performed by two of the authors (S.M. with either K.M., D.J. or U.W.) who were blind to the neurocognitive performance of the patients at the time of the psychopathological assessment.

In accordance with Spitzer, schizophrenic subjects who scored high on the 'associative loosening' item of the PANADSS (score: 3 (mild) to 7 (extremely severe)) were further labelled as positive thought-disordered (TD), subjects below that range were characterized as non-positive thought-disordered (NTD).

Semantic priming procedure

The semantic priming task was presented on Macintosh/Apple computers (Macintosh Classic or LC II). Program and stimuli were identical to previous experiments conducted by Spitzer and colleagues. Four different conditions were set up: (*a*) unrelated condition (18 trials, e.g. sofa – wing); (*b*) semantic priming condition (18 trials, e.g. hen – egg); (*c*) indirect semantic priming condition (18 trials, e.g. lemon – sweet); and, (*d*) non-word condition (54 trials, e.g. drift – kribe).

Word pairs (font Geneva, point 18) were derived from different published lists of (normed) associations (De Groot, 1983; Balota & Lorch, 1988; McNamara & Altarriba, 1988). Stimuli were between three and nine characters long (mean: 5·1 characters). Non-words were all legally spelled. Two strings of letters were successively presented in each trial (prime, German word; probe, German word or non-word). Prior to the presentation of each trial, the computer screen was blank. Once a trial was initiated via mouse-click (self-paced by the participant), a small fixation point appeared for 700 ms in the centre of the computer screen followed by the prime. The prime occurred for 200 ms and was immediately followed by the probe resulting in a stimulus onset asynchrony of 200 ms (sensitive to the measurement of automatic spreading of activation). The probe was displayed until the response was executed. The subjects' task was to read the first word silently (i.e. the prime) and to respond as fast as possible to the second string (i.e. the probe) without making too many mistakes. Trials required a lexical decision after the presentation of the second string. The key 'n' had to be pressed using the index or middle finger of the dominant hand if subjects thought that a non-word was shown. By pressing the key 'b', the participant indicated that the second string was a regular German word.

Before starting the actual experiments, subjects performed a brief practice task consisting of 24 trials. Trials with false reactions were not submitted to further statistical analysis. RT outliers were rejected following the procedure adopted by Spitzer: RTs greater than twice a given subject's mean RT for a particular condition were excluded from further analysis. Subsequent analyses relied on mean RTs.

RESULTS

Impact of psychomotor slowing on priming

Following Chapman *et al.* (1994), the influence of psychomotor slowing on the semantic priming effect was determined by inspecting data obtained in a large sample of healthy subjects ($N = 160$; see Moritz *et al.* 1999). Using linear and non-linear regression, psychomotor slowing (summed up RTs of all conditions) did not explain semantic ($R = 0{\cdot}06$) or indirect semantic priming ($R = 0{\cdot}04$) for a 200 ms SOA condition identical to that of the present study. However, for a semantic priming condition favouring controlled processes (SOA, 700 ms), not performed in the present study, a significant correlation emerged (indirect semantic priming, $R = 0{\cdot}34$ ($P \leqslant 0{\cdot}0001$); semantic priming, $R = 0{\cdot}29$ ($P \leqslant 0{\cdot}0005$)). Both regression coefficients for the short SOA task were 0·0, so that the index

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Table 2. *Reaction times (mean and standard deviations) and error rates of the (sub-)samples*

	Schizophrenics (S) ($N = 44$)			NTD ($N = 28$)			TD ($N = 16$)			Healthy controls (H) ($N = 30$)			Psychiatric control (P) ($N = 36$)			
	RT		Error	RT		Error	RT		Error	RT		Error	RT		Error	
Condition	Mean	S.D.	%	Mean	S.D.	%	Mean	S.D.	%	Mean	S.D.	%	Mean	S.D.	%	Group comparisons *post-hoc* (Newman–Keuls)
Independent	831·1	202·8	5·3	768·0	134·1	2·8	941·5	255·1	4·5	727·9	165·6	3·7	827·7	238·7	2·8	
Non-word	915·1	301·1	4·5	876·0	322·0	3·2	983·4	255·6	4·4	805·5	206·7	5·4	959·2	315·1	3·2	
Semantic	756·0	182·4	2·0	712·4	137·7	1·2	832·4	226·8	3·5	656·2	126·7	1·3	775·0	251·1	1·2	
Indirect semantic	766·3	165·5	3·5	719·8	129·2	0·9	847·8	193·3	5·9	688·7	142·3	1·1	809·9	229·0	0·9	
SP	−75·1	99·8		−55·6	52·4		−109·1	147·2		−71·7	59·1		−52·7	75·6		S = H = P; TD < NTD/P†
Paired *t* tests	****			****			**			****			****			
ISP	−64·8	79·6		−48·2	46·4		−93·7	113·6		−39·2	63·5		−17·8	67·4		S < P; TD < NTD/H/P
Paired *t* tests	****			****			***			***			(NS)			

* $P \leqslant 0{\cdot}05$; ** $P \leqslant 0{\cdot}01$; *** $P \leqslant 0{\cdot}005$; **** $P \leqslant 0{\cdot}001$.

SP, semantic priming difference score; ISP, indirect semantic priming difference score; TD, positive thought-disordered schizophrenic subjects; NTD, non-positive thought-disordered schizophrenic subjects.

† TD patients differed from NTD patients and psychiatric controls at trend level.

D (adjusted difference score) of the equation to compute difference scores (Chapman *et al.* 1994) remained unchanged for indirect and direct semantic priming effects.

Indirect semantic priming

Comparison between schizophrenic patients (whole sample) and controls

A two-way ANOVA with conditions as within-subject variable (independent, direct and indirect semantic condition) and diagnosis (schizophrenic patients, healthy and psychiatric control group) as group variable and RT as the dependent variable revealed that the effects of condition ($F(2, 107) = 42{\cdot}92$; $P \leqslant 0{\cdot}001$) and diagnosis ($F(2, 107) = 3{\cdot}52$; $P \leqslant 0{\cdot}05$) turned out to be significant. The interaction achieved trend level ($F = 2{\cdot}26$; $P = 0{\cdot}06$). As can be deduced from Table 2, the significant result obtained for diagnosis is attributable to the slowed down RTs of both psychopathological groups. The significant condition effect reflects different performance baselines for all conditions (RTs, independent condition > indirect semantic priming condition > (direct) semantic priming condition).

For evaluating *post-hoc* comparisons the (adjusted) priming difference score (independent condition minus experimental condition (either semantic priming or indirect semantic priming condition)) between the three groups were entered. The overall *F* test achieved significance ($F(2, 108) = 4{\cdot}40$; $P \leqslant 0{\cdot}01$). Schizophrenics ($M = -64{\cdot}8$ ms) as a whole group showed significantly enhanced indirect semantic priming as compared to psychiatric ($M = -17{\cdot}8$ ms) but not healthy controls ($M = -39{\cdot}2$ ms). Both control groups did not differ with regard to indirect semantic priming. Although schizophrenics displayed more (direct) semantic priming ($M = -75{\cdot}1$ ms) than healthy and psychiatric controls ($M = -71{\cdot}7$ ms, $M = -52{\cdot}7$ ms), *post-hoc* tests did not reveal any significant results (overall $F(2, 108) = 0{\cdot}84$; $P > 0{\cdot}4$).

Simple paired *t* tests showed that all groups exhibited significant semantic priming. With the exception of the psychiatric control group ($P = 0{\cdot}16$), the indirect semantic priming effect achieved significance for all groups and schizophrenic sub-samples.

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Comparison between TD and NTD schizophrenic patients and controls

Sixteen of the schizophrenic subjects showed at least mild but clearly detectable forms of associative loosening (positive thought-disordered group (TD)), 28 of the patients were characterized as non-positive thought-disordered (NTD). A two-way ANOVA revealed significant effects for condition ($F(2, 107) = 50{\cdot}61$; $P \leqslant 0{\cdot}001$), diagnosis ($F(2, 107) = 4{\cdot}19$; $P \leqslant 0{\cdot}01$), and the interaction of condition and diagnosis ($F = 2{\cdot}47$; $P \leqslant 0{\cdot}05$). When applying this dichotomy in a one-way ANOVA with priming-effect (semantic/indirect semantic priming effect) as the dependent variable, the TD group significantly differed from the healthy ($P \leqslant 0{\cdot}05$) and the psychiatric control group ($P \leqslant 0{\cdot}005$) as well as the NTD group ($P \leqslant 0{\cdot}05$) with regard to indirect semantic priming. No other differences achieved significance.

For (direct) semantic priming, no group differences turned out to be significant using the Student–Newman–Keuls procedure. However, TD patients differed at trend level from psychiatric controls ($P = 0{\cdot}09$) and NTD patients ($P = 0{\cdot}10$). The difference between TD patients and healthy controls failed trend level ($P = 0{\cdot}14$).

Impact of potential confounding variables on (indirect) semantic priming

Neither the length of the schizophrenic illness nor age (all groups entered), nor years of school (all groups entered), modulated semantic and indirect semantic priming ($r \leqslant 0{\cdot}15$ for all correlations, NS). Chlorpromazine equivalents did not significantly correlate with semantic ($r = 0{\cdot}12$, NS) and indirect semantic priming ($r = 0{\cdot}06$, NS).

Finally, to rule out general schizophrenic psychopathology as the cause of increased priming effects in the TD group, both groups were compared with regard to their overall psychopathology (PANADSS-global score without symptoms of positive formal thought disorder). Although TD displayed significantly increased psychopathology as compared to the NTD group (41·2 *versus* 33·6; $P \leqslant 0{\cdot}05$), semantic and indirect priming were not different when subjects were split according to the median of the overall psychopathology (for indirect semantic priming, low psychopathology group $-61{\cdot}7$ ms; high psychopathology group $-64{\cdot}9$ ms; $t(41) = 0{\cdot}13$; $P > 0{\cdot}8$; for semantic priming, low psychopathology group $-65{\cdot}8$ ms; high psychopathology group $-83{\cdot}4$ ms; $t(42) = 0{\cdot}57$; $P > 0{\cdot}5$).

Concerning error rates, no significant differences occurred among groups (controls *versus* the entire schizophrenic group ($F(2, 107) = 2{\cdot}14$, NS) and both subgroups, respectively ($F(3, 106) = 1{\cdot}53$, NS)). There was no indication of a speed-accuracy trade-off since overall RTs and error rates did not significantly correlate (all subjects $r = 0{\cdot}00$; healthy controls $r = -0{\cdot}18$; $P > 0{\cdot}3$; schizophrenic sample $r = 0{\cdot}16$; $P > 0{\cdot}3$; psychiatric controls $r = -0{\cdot}07$; $P > 0{\cdot}6$).

DISCUSSION

Schizophrenic patients (as a whole group) displayed significantly enhanced indirect semantic priming (hyper-priming) when compared with psychiatric but not with healthy controls. When the schizophrenic group was split with regard to the presence or absence of associative loosening, in line with previous research (Spitzer, 1993*a*; Weisbrod *et al.* 1998) the results remained significant only for the thought-disordered group. Our results demonstrate that positive formal thought disorder is marked by disinhibited semantic networks. In line with Spitzer (1997) it is inferred that an excessive spread of activation (as assessed with the indirect semantic priming procedure) is the cognitive correlate of positive formal thought disorder (loosening of associations, tangential speech). Thus, indirect semantic priming may serve as a candidate marker of schizophrenic patients who suffer from positive thought disorder. Future research using a longitudinal approach will have to show whether indirect semantic priming is a stable vulnerability, mediating vulnerability, or episode marker of schizophrenic psychopathology according to the rationale laid down by Nuechterlein and co-workers (1994).

Several variables that have been suggested to contribute to semantic priming did not modulate the effect in this study: neither length of illness nor age nor neuroleptic dose correlated with priming. It should be noted, however, that the results of Maher *et al.* (1996), which suggest an inverse relationship between length of illness

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and priming, were obtained in a more chronic sample. In addition, since 41 of the 44 schizophrenic patients were either treated with atypical neuroleptics or were unmedicated at the time of testing, parkinsonoid symptoms (i.e. side-effects of conventional neuroleptics like haloperidol) did not contribute to the results.

Moreover, linear and non-linear regression confirmed that semantic and indirect semantic priming cannot be considered an artefact of psychomotor slowing. Furthermore, our design employed a task that clearly tapped automatic spreading activation as the stimulus onset asynchrony was far below 500 ms.

As a valuable result for cognitive research, we were able to replicate a previous result (Moritz *et al*. 1999), that indirect semantic priming as measured in a lexical decision task reliably occurs in healthy subjects. Previous research (see Neely, 1991) has found stable indirect semantic priming preferably in word pronunciation tasks.

Although TD schizophrenics displayed enhanced semantic priming as compared to NTD and controls, group differences only achieved trend level for two out of three comparisons. Although some studies have found significantly (for example, Baving, 1998; Kwapil *et al*. 1990) or insignificantly (Henik *et al*. 1995) enhanced semantic priming in schizophrenics, more recent research emphasizes that direct semantic priming may not be the best procedure to evaluate the issues raised. Spitzer (1993*a*) writes: 'However, if "heightened activation" not only implies "faster spread" but also "further spread" of activation in the semantic network, then the prediction can be derived that far associations – instead of close associations – should be a more effective discriminator between normal and activated associative networks' (page 867). Therefore, further studies on the neurocognitive correlates of formal thought-disorder should employ indirect semantic priming rather than (direct) semantic priming conditions.

We suspect that those studies reporting attenuated, or less semantic priming, in (thought-disordered) schizophrenics suffered from at least one of the following methodological flaws: SOAs above or at the border of automatic processing (Besche *et al*. 1995; Passerieux *et al*. 1997; contrary to their rationale, Aloia *et al*. 1998, employed a semantic priming procedure favouring controlled processes); small sample (Blum & Freides, 1995; the variability of the performance of schizophrenics calls for large samples); short prime display times (Vinogradov *et al*. 1992; Blum & Freides, 1995; Ober *et al*. 1995, 1997; Barch *et al*. 1996); no investigation of thought-disordered subtypes (for example, Chapin *et al*. 1989, 1992); and, inadequate design (Passerieux *et al*. 1995, did not find reliable semantic priming even in healthy controls). Moreover, although length of illness and semantic priming did not correlate in our schizophrenic sample, the results obtained by Maher *et al*. (1996) and our results concerning psychiatric controls suggest that this variable has to be further considered as a contributor to decreased semantic priming, especially in chronic samples.

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