

Relapse in Young Paranoid Schizophrenic Patients: A Prospective Study of Stressful Life Events, P300 Measures, and Coping

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***Objective:** The authors investigated the relationship of cognitive and coping characteristics to stressful life events at the time of relapse in patients with recent-onset paranoid schizophrenia. **Method:** Over 6 years, the authors collected data on 41 schizophrenic outpatients aged 18–28 years at recruitment. The patients were rated prospectively every 2 weeks with the Brief Psychiatric Rating Scale, Scale for the Assessment of Negative Symptoms, Scale for the Assessment of Positive Symptoms, Global Assessment of Functioning Scale, and life events measures. The Frankfurt Questionnaire of Complaints was used to analyze subjective complaints regarding cognitive and coping abilities. The P300 auditory event-related potential was measured at recruitment to provide an index of information-processing capability. **Results:** Patients without severe life events during the 1 month before relapse had a smaller P300, more subjective complaints, and less coping capacity than did relapsed schizophrenic subjects who had severe life events in the month before relapse. **Conclusions:** Relapses in subjects without severe life events were associated with fewer cognitive resources and less coping ability. Patients with normal P300 and adequate coping resources seemed to be able to deal better with stressful life events.*

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The role of independent life events in schizophrenic relapses has been well documented in both retrospective (1, 2) and prospective (3, 4) studies. However, what deserves further consideration is that at least 50% of the instances of schizophrenic relapse occur without any increase in major life events in the preceding 1-month period (4, 5), suggesting that these patients may experience acute accentuations of vulnerability to relapse as a result of natural oscillation in their biological systems (4). To our knowledge, to date there have been no investigations relating the cognitive characteristics of schizophrenic subjects to the level of stress at the time of relapse, and the aim of the present study was to start to fill this gap.

Schizophrenic vulnerability (comprising, for example, certain cognitive dysfunctions and specific coping limitations) may be associated with sensitivity to socioenvironmental stress factors that lift the individual's susceptibility over the threshold beyond which an exac-

erbation of psychotic symptoms or a relapse can be expected (6, 7).

One serious difficulty in carrying out this kind of study relates to the process of assessing and determining the degree of reliability of the recollection of life events during the course of the disease. To avoid the common biases that can occur in this kind of research, a series of measures were adopted: prospective research with follow-up analysis, schizophrenic subtyping (in order to avoid producing results that cannot be extended to an entire schizophrenic subpopulation), the use of appropriate criteria to define relapse, and the use of appropriate instruments for the assessment of stressful life events, such as Brown and Harris's Life Events and Difficulty Schedule (8), which was conducted by a trained expert.

In their ongoing longitudinal study of developmental processes in schizophrenia, Nuechterlein et al. (5, 9) focused on several information-processing neuropsychological and neurophysiological indexes ("stable vulnerability indicators"), but they did not consider each subject's coping strategies and the level of subjective experiences, nor did they consider the P300 event-related potential, which is one of the most reliable indexes of information-processing dysfunction (10–12).

Moreover, lower rates of relapse (13, 14) have been associated with a small P300 amplitude in schizophrenic patients.

We may hypothesize that this susceptibility to stress

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is the result of both information-processing abnormalities and maladaptive coping mechanisms and strategies used by the patient (15). In fact, it is well known that schizophrenic subjects attempt to deal with certain consequences of vulnerability by using self-protective coping strategies, with varying degrees of success. The effectiveness or otherwise of such compensatory strategies may play an important role in preventing, or failing to prevent, a psychotic breakdown (16).

To our knowledge, this is the first prospective study to examine the correlation of cognitive and coping characteristics with stressful life events before relapse in a homogeneous schizophrenic study group. Although possible information-processing abnormalities are relatively accessible through neurophysiological techniques, in investigating coping we had to venture beyond the "shadow line" of information processing, to include an assessment of subjective cognitive strategies.

METHOD

Subjects

The initial study group consisted of 53 outpatients recruited, after giving written informed consent, on a rolling basis at the Institute for Neurosciences in Florence beginning in March 1990 (17). From the initial group, 41 right-handed outpatients (31 male, 10 female) were considered; they fulfilled the DSM-III-R criteria and Research Diagnostic Criteria (18) for schizophrenic disorder, paranoid type. Their mean age was 23.7 years ($SD=3.6$, range=18–28), and they had an initial onset of psychosis no more than 30 months before recruitment. The mean duration of illness at the time of recruitment was 1.7 years ($SD=1.2$), and the mean number of weeks of prior hospitalization was 10.2 ($SD=4.4$). The mean educational level of the patients was 10.9 years ($SD=2.8$). The exclusion criteria were signs of tardive dyskinesia, concomitant medical diseases, substance abuse (investigated through biological tests when suspected in the clinical interview), and previous ECT. The patients' IQs, as measured by the WAIS, were normal. No patient received lithium or carbamazepine, and all patients were receiving neuroleptic treatment during follow-up. At the time of neurophysiological and clinical investigation the mean dose in chlorpromazine equivalents per day was 204.7 mg ($SD=97.4$); at relapse the mean neuroleptic dose was 211.3 mg. The comparison group consisted of 41 right-handed age- and sex-matched healthy volunteers recruited from the community (mean age=24.9 years, $SD=4.3$). None had a personal or family history of psychiatric disorders, relevant medical diseases, or drug abuse.

Clinical Evaluations

Clinical ratings. Clinical assessment was conducted by using the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms (SANS) and the Scale for the Assessment of Positive Symptoms (SAPS) (19), and the Global Assessment of Functioning Scale (DSM-III-R). Every 2 weeks after recruitment, an experienced psychiatrist rated the patient's clinical state with these measures. The raters were blind to the results of the psychophysiological analysis. The method of Ventura et al. (4) was used to determine psychotic relapse and exacerbation, and these two categories were combined in the analyses. Scores on three BPRS subscales (unusual thought content, hallucinations, conceptual disorganization) were considered in order to define the following.

1. Psychotic relapse: a rating of 6 or 7 on any of the three scales after the patient had been in remission (score of 3 or below) for at least 1 month.

2. Major psychotic exacerbation following a state of remission: a rating of 5 plus an increase of 2 points on one of the other two scales,

or a rating of 5 on any of the three scales for more than two consecutive 2-week BPRS ratings.

3. Major psychotic exacerbation following a state of persisting psychotic symptoms: an increase of 2 or more points to a scale rating of 6 or 7, or a 1-point increase on any scale to a rating of 6 or 7 plus an accompanying 2-point increase on one of the other two scales.

Assessment of life events. Life events were assessed in the patient group every 2 weeks after recruitment by using the open-ended questions of Brown and Harris (8) to determine whether an event was of sufficient magnitude or associated with sufficient change in role status to be categorized as a life event. The healthy subjects were assessed for life events at recruitment but not during follow-up. This evaluation was conducted by a certified psychiatrist (S.P.), following specific training from Brown and Harris, using the procedure for collecting and rating life events described elsewhere by Faravelli and Pallanti (20). The interviewers were aware of the patient or comparison status of the subjects, but the assessor was not: he received randomly mixed reports and was not involved in the interviews. Any element that could permit identification was omitted. A 4-point scale was used to rate the threat the average person would see in the event: 1=marked threat, 2=moderate threat, 3=mild threat, 4=no threat.

The normative list of life events of Paykel et al. (21) was also used in order to provide measurable indexes of stressful events (number of events, weighted scores for all events, subjects with at least one severe event) in the 3 months preceding relapse. Ratings of 1 and 2 on the Brown and Harris assessment and the 20th-ranked event on the scale of Paykel et al. ("loss of personally valuable object") were considered the cutoff points to distinguish severe from nonsevere events, and events were classified as "dependent" (i.e., under the control of the subject or related to the illness) or "independent" (i.e., unexpected and not determined by the subject's behavior) (22). For instance, an event such as "sudden stroke of father" was considered unlikely to be determined by the subject and was thus assessed as independent. On the other hand, events such as "loss of job because of absenteeism" were considered dependent, since they were possibly secondary to disordered behavior on the part of the subject.

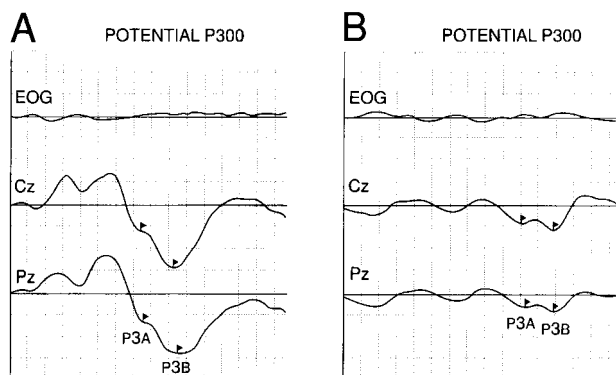
Cognitive Evaluations

Objective: P300 testing. At recruitment the P300 auditory evoked potential (P3b component) in the patients and normal subjects was obtained by means of a simple "oddball" paradigm. Two successive series of randomly intermixed tones (1000 Hz, overall probability 85%; 2000 Hz, probability 15%) were delivered binaurally through earphones at a rate of one tone (70-dB sound level, 50-msec duration) every 1.1 seconds. The subjects were required to keep a mental count of the rare tones and to report the number at the end of each series. The responses were recorded (filter bandpass: 0.1–100 Hz) from scalp Ag/AgCl Fz, Cz, and Pz electrodes, all referring to linked mastoids. The Fz electrode registrations were excluded from the statistical analyses because of a generalized smaller amplitude of the P3b component that is less useful in comparing groups and because of the desire to minimize the risk of ocular artifacts on the tracks. Eye movements were monitored through electrodes on the nasion and on the left zygomatic bone. The responses to the frequent ($N=100$) and rare ($N=28-30$) tones were averaged separately and stored on flexible diskettes for off-line analysis. Trials containing eye movement artifacts of 100 μV or more were automatically rejected. The peak latency and peak-to-peak amplitude of P3b in response to the rare tone were measured in all the electrodes (figure 1).

Subjective: experienced disturbances and coping. The Frankfurt Questionnaire of Complaints (23, 24) is a measure for self-evaluation of subjective disturbing experiences of cognitive impairment. It was used with both the patients and healthy subjects. It consists of 98 statements (yes/no answers) organized according to four dimensions of the disturbance, as established by Süllwold and Huber (23) from factor analysis: 1) disorders of normally automatic skills, 2) perceptual disorders, 3) depression/anhedonia, and 4) stimulus overload.

To investigate coping, we extracted a short 20-item version of the questionnaire, with five items per dimension, that satisfied the criteria of a high loading on one of the dimensional factors, and it was used according to the method applied by Wiedl and Schöttner (25). In a subsequent semistandardized interview, the patients were asked what

FIGURE 1. P300 Auditory Evoked Potential (Cz, Pz) and Electro-Oculogram (EOG) for (A) a Healthy Subject and (B) a Relapsed Schizophrenic Patient Who Did Not Have Any Severe Independent^a Life Events in the 1 Month Before Relapse



^aUnexpected and not determined by the patient's behavior.

strategies helped them to cope with the basic disturbances covered in the questionnaire.

Questions were formulated from a list given to the interviewer (e.g., "How do you cope with this situation?" and "How do you handle or manage this problem?"). This procedure was applied for each of the 20 items in the shortened Frankfurt Questionnaire of Complaints to which the subject responded affirmatively. The patients were also asked to rate on a 5-point scale how effective their efforts were in coping with the respective stresses. The interviewer's written reports on the patients' answers were also evaluated by two expert psychiatrists separately, to identify the directivity and the level of coping strategies. For each basic symptom, the coping efforts were classified as "problem-centered" (directly aimed at modifying or eliminating the source of interference) or "non-problem-centered" (maintaining distance from whatever is experienced as stressful, i.e., withdrawal, avoidance, suppression, or other ineffective cognitive coping reaction), according to the method adopted by Brenner et al. (26). Three further types of coping strategy were considered: behavioral (externally observable actions), cognitive (inner coping processes), and emotional (affective reactions). Assessment of the clinical ratings and coping characterization was conducted by three experienced psychiatrists including S.P. and L.Q.). Interrater reliability was assessed every 12 months and consistently ranged between 0.75 and 0.90 (Cohen's kappa). Concordance on the Frankfurt Questionnaire of Complaints, determined for a 10-patient randomly selected subgroup, was never less than 79%.

Statistical Analysis

One-way analysis of variance (ANOVA), ANOVA for repeated measures, the paired t test, and the chi-square test were performed

where appropriate to assess the significance of differences between groups, with alpha set at $p < 0.05$, two-tailed. The data were analyzed by using the SPSS/PC package (27), running on a 33-MHz 486 personal computer.

RESULTS

Of the initial 53 patients, 12 (22.6%) were excluded from the analysis: five dropped out and seven did not relapse during the follow-up period (mean=26.3 weeks, SD=11.2).

At the time of relapse, the mean clinical scores were as follows: BPRS, 51.2 (SD=7.4); SAPS (sum of global scores), 13.5 (SD=2.1); and SANS (sum of global scores), 9.8 (SD=3.8).

The entire group was analyzed for stressful life events in the 3 months preceding relapse. The mean score on the Paykel life events scale for the schizophrenic patients was 20.9 (SD=5.0), while the mean score for independent life events in the same period was 13.1 (SD=4.5). As shown in table 1, the magnitude of stressful life events, especially independent ones, increased in the 13 weeks before relapse, but the scores increased especially during the 4 weeks before the psychotic episodes (table 1).

For further analysis, two subgroups were formed from the relapsed schizophrenic patients: the 25 patients (61.0%) who had at least one severe independent life event (Brown and Harris rating of 1 or 2; rank of 1-20 on scale of Paykel et al.) in the 1 month before relapse and the 16 patients who did not (39.0%). Table 2 compares the demographic, neurophysiological, and clinical characteristics of the two subgroups.

No differences were found between the two subgroups in terms of age, sex, and clinical state (BPRS, SANS, and SAPS scores). Patients who had had at least one severe independent life event in the 1 month before relapse had a significantly higher educational level and global functioning score in the last year (table 2), a markedly and significantly higher P300 (P3b component) amplitude (table 3), and a nonsignificantly lower P300 latency (table 3).

The schizophrenic patients showed significantly longer P300 latencies and smaller amplitudes than the healthy subjects (table 3). However, the patients who had at least one severe independent life event in the month before re-

TABLE 1. Magnitude of Life Events in Three 1-Month Periods Before Relapse for 41 Schizophrenic Patients

Type of Life Event	Score on Scale of Paykel et al. (21)						ANOVA for Repeated Measures (df=2, 40)	
	90-61 Days Before Relapse		60-31 Days Before Relapse		30-1 Days Before Relapse		F	p
	Mean	SD	Mean	SD	Mean	SD		
All	17.0	9.3	18.6	8.5	26.9 ^a	12.9	10.63	<0.001
Independent ^b	10.4	5.1	11.7	7.7	18.2 ^c	9.2	12.59	<0.001

^aSignificantly different from preceding 1-month period (paired t test; $t=3.21$, $df=40$, $p < 0.01$).

^bUnexpected and not determined by the patient's behavior.

^cSignificantly different from preceding 1-month period (paired t test; $t=3.16$, $df=40$, $p < 0.01$).

TABLE 2. Characteristics of Relapsed Schizophrenic Patients With and Without at Least One Severe Independent^a Life Event in the 1 Month Before Relapse

Baseline Characteristic	Patients With Severe Life Events (N=25)		Patients Without Severe Life Events (N=16)		Analysis	Total Group (N=41)	
	N		N		χ^2 (df=1)	N	
Sex					0.08		
Female	8		5			13	
Male	17		11			28	
	Mean	SD	Mean	SD	F (df=1, 40)	Mean	SD
Age (years)	24.2	4.1	22.6	3.4	1.69	23.7	3.6
Educational level (years)	11.6	2.8	9.7	2.7	4.58*	10.9	2.8
Score on Global Assessment of Functioning Scale (for previous year)	61.8	12.9	51.4	13.6	6.06*	57.7	13.2
BPRS total score	31.8	6.5	35.2	8.3	2.20	33.1	7.2
SAPS score (sum of global scores)	4.6	1.9	5.2	2.1	0.75	4.8	2.0
SANS score (sum of global scores)	8.8	2.7	9.2	2.5	0.17	9.0	2.6

^aUnexpected and not determined by the patient's behavior.

*p<0.05.

lapse showed less difference from the healthy subjects in P300 latencies than did the patients without severe life events, and they showed no significant difference from the healthy subjects in Cz-electrode P3b performance.

Table 4 shows subgroup and overall scores on the Frankfurt Questionnaire of Complaints, the questionnaire used to assess subjective disturbances. The patients who did not have any severe independent life events in the 1 month before relapse had higher scores on most measures than the patients who had at least one severe independent life event during this period; the difference was especially great for the fourth factorial dimension of basic disturbances (external and internal overstimulation).

The comparison subjects had a much lower total score on the Frankfurt Questionnaire of Complaints (mean=6.4, SD=4.9) than did the patients (mean=46.6, SD=16.3) (t=15.11, df corrected for unequal variances=47, p<0.001), and the scores on the subscales were also much lower than those of the patients (data not shown).

The reduced version of the Frankfurt Questionnaire of Complaints (20 high-loading items) was then extracted, to permit easier investigation of coping mechanisms; the results are shown in table 5. The patients who had at least one severe independent life event in the 1 month before relapse had a significantly higher rate of problem-centered coping strategies than did the pa-

TABLE 3. Amplitude and Latency of P300 Auditory Evoked Potential for Relapsed Schizophrenic Patients With and Without at Least One Severe Independent^a Life Event in the 1 Month Before Relapse and for Healthy Subjects

P300 Measure	Schizophrenic Patients						Healthy Subjects (N=41)	
	With Severe Life Events (N=25)		Without Severe Life Events (N=16)		Total (N=41)		Mean	SD
	Mean	SD	Mean	SD	Mean	SD		
Amplitude (µV)								
Cz	12.7 ^b	4.6	7.5 ^c	3.2	10.6 ^d	4.1	15.5	6.5
Pz	13.4 ^e	5.1	9.4 ^c	4.6	11.9 ^d	4.9	16.9	6.2
Latency (msec)								
Cz	344.1 ^f	45.4	367.3 ^c	49.0	353.1 ^g	46.8	317.2	25.0
Pz	348.3 ^f	45.7	368.7 ^c	47.2	356.3 ^g	46.3	319.4	25.8

^aUnexpected and not determined by the patient's behavior.

^bSignificantly different from patients without severe life events (one-way ANOVA; p<0.0001, df=1, 40).

^cSignificantly different from healthy subjects (one-way ANOVA; p<0.0001, df=1, 56).

^dSignificantly different from healthy subjects (one-way ANOVA; p<0.01, df=1, 81).

^eSignificantly different from patients without severe life events (p<0.05, df=1, 40) and from healthy subjects (p<0.05, df=1, 65) (one-way ANOVA).

^fSignificantly different from healthy subjects (one-way ANOVA; p<0.01, df=1, 56).

^gSignificantly different from healthy subjects (one-way ANOVA; p<0.0001, df=1, 81).

tients who did not have any severe independent life events, and they showed significantly more effective behavioral and cognitive coping. In particular, the patients who did not have any severe independent life events in the month before relapse reacted with behavioral coping to basic disturbances in 60.9% of the situations but exhibited a high occurrence of failure in behavioral coping directivity (67.0% of all behavioral coping). Globally, they showed a predominance of non-problem-centered coping, whereas the patients who did experience severe life events before relapse used non-problem-centered coping in fewer than one-half of the instances. No significant differences were found in emotional coping responses between the two subgroups.

TABLE 4. Subjective Cognitive Disturbances in Relapsed Schizophrenic Patients With and Without at Least One Severe Independent^a Life Event in the 1 Month Before Relapse

Measure From the Frankfurt Questionnaire of Complaints (23, 24)	Score (number of affirmative answers)				F (df=1, 40)	Score of Total Group (N=41)	
	Patients With Severe Life Events (N=25)		Patients Without Severe Life Events (N=16)			Mean	SD
	Mean	SD	Mean	SD			
Total (98 statements)	41.6	14.7	54.3	15.2	7.06*	46.6	16.3
Automatic skills (22 statements)	11.2	5.4	15.0	6.2	4.28*	12.7	5.7
Perceptual disturbance (30 statements)	10.0	5.1	11.9	5.9	1.14	10.7	5.6
Anhedonia (27 statements)	16.2	5.0	15.2	4.1	0.37	15.8	4.7
Overstimulation (18 statements)	9.0	4.2	15.6	5.7	18.02**	11.6	4.7

^aUnexpected and not determined by the patient's behavior.

*p<0.05. **p<0.01.

TABLE 5. Coping Efforts by Relapsed Schizophrenic Patients With (N=25) and Without (N=16) at Least One Severe Independent^a Life Event in the 1 Month Before Relapse

Coping Strategy and Directivity of Coping ^b	Instances of Coping Strategy				χ^2 (df=1)	Instances of Coping Strategy for Total Group (380 coping efforts)	
	Patients With Severe Life Events (201 coping efforts)		Patients Without Severe Life Events (179 coping efforts)			N	%
	N	%	N	%			
Behavioral coping					7.50**		
Problem-centered	57	28.4	36	20.1		93	24.5
Non-problem-centered	52	25.9	73	40.8		125	32.9
Cognitive coping					5.64*		
Problem-centered	48	23.9	18	10.1		66	17.4
Non-problem-centered	18	9.0	20	11.2		38	10.0
Emotional coping					1.49		
Problem-centered	14	7.0	11	6.1		25	6.6
Non-problem-centered	12	6.0	21	11.7		33	8.7
Total					18.96***		
Problem-centered coping	119	59.2	65	36.3		184	48.4
Non-problem-centered coping	82	40.8	114	63.7		196	51.6

^aUnexpected and not determined by the patient's behavior.

^bProblem-centered coping was activity directly aimed at modifying or eliminating the source of interference. Non-problem-centered coping was a reaction that maintained distance from whatever was experienced as stressful, i.e., withdrawal, avoidance, suppression, or other ineffective cognitive coping reaction.

*p<0.05. **p<0.01. ***p<0.001.

DISCUSSION

The main finding of the present study is that schizophrenic patients who relapsed without the occurrence of severe stressful life events in the preceding month manifested a significantly lower P300 amplitude and significantly more complaints of subjective cognitive dysfunction but also more dysfunctional coping strategies than schizophrenic patients who had at least one severe independent life event in the 1 month before relapse.

The percentages of patients who relapsed with (61.0%) and without (39.0%) severe life events are similar to previous results from both retrospective (2) and prospective (4, 28, 29) studies.

The clinical characteristics of the study group (outpatients, young age, recent onset of the disease, psychotropic drug use), the diagnostic subtype (paranoid), and

the relatively good social adaptation should enable us to avoid the "floor effect" related to social disconnection (which involves a reduction of social events) and to permit assessment of intragroup discrimination reliability.

The present findings lend support to our working hypothesis that differences in how patients deal with life events may be mediated by complex cognitive and coping capacities and that relapses in patients possessing better-preserved information-processing ability and more-effective coping strategies (while taking psychotropic medication) could be significantly related to additional stress resulting from life events.

P300 abnormalities have been related to clinical characteristics, such as residual symptoms (30), positive (31) or negative (32, 33) symptoms, thought disorder scores (34), higher risk for tardive dyskinesia (14), and poor outcome (13, 14), but the data from the studies on outcome are controversial. Hegerl et al. (14) reported a

low relapse rate in a group of schizophrenic patients with a small P300 amplitude and concluded that small P300 amplitude could indicate a more chronic course and an unfavorable outcome in these patients, a view in line with a previous suggestion by Murray et al. (13). However, the conclusion of Hegerl et al. is based on results obtained from chronically ill schizophrenic patients (whose reports have low reliability) and, moreover, is not entirely supported by the results themselves, which lack statistical significance (the relapse rate among patients with P300 amplitudes larger than 4.9 μ V was 13 of 44, and the rate among patients whose P300 amplitudes were smaller than 4.9 μ V was seven of 44). The use of unstandardized and nonspecific relapse criteria such as "hospitalization" (mean number of prior hospitalizations=3.1, range=1-16) has to be considered another form of bias.

A limitation of the present study was that P300 was assessed only in the recruitment stage. Assessment at the time of relapse, although it might have been difficult because of poor cooperation by patients in the recording of event-related potentials, would be useful for the evaluation of possible changes. As P300 changes have been documented in association with clinical improvement (35) resulting from neuroleptic treatment (36-38), we cannot exclude the possibility that the patients' good P300 performance and subsequent resistance to stress may be effects of the treatment. However, this does not undermine the importance of the research results; indeed, it highlights the importance of evaluating cognitive features both in relation to the response to neuroleptics and in the different phases because it would provide information about a clinically homogeneous study group such as ours. In fact, there is evidence that the P300 amplitude does not change significantly after neuroleptic treatment (39, 40).

It remains to be seen whether small P300 amplitude should be considered as a trait or a phase index of cognitive susceptibility to stress.

While our schizophrenic patients did not differ from the normal subjects in earlier phases of event-related potentials, it would be interesting to focus on the characteristics of the endogenous negativity through other tasks, such as a simple response task and a discriminative response task (41), to permit a more specific evaluation of cognitive processing.

In the present study patients who did not have any severe independent life events in the 1 month before relapse exhibited a higher rate of subjective complaints (so-called basic symptoms) and a smaller capacity for and less effectiveness of self-generated coping strategies than patients who did have severe life events in the preceding month, and the patients without severe life events also had a significantly smaller P300 amplitude.

A correlation between subjective experience of cognitive disturbances and event-related potentials has already been reported: van den Bosch and Rozendaal (42) found that a subjective disturbance score, not clinical ratings, showed significant associations with psychophysiological measures (contingent negative variation,

reaction time). In contrast, our schizophrenic patients who had at least one severe independent life event in the 1 month before relapse had normal P300 measures and had a lower score for subjective complaints and greater use of problem-centered coping strategies than patients without severe life events.

The concept of coping corrects the image of the schizophrenic patient as a person who is passive and helpless in the face of his or her illness; in fact, a self-perception of cognitive abnormalities leads the patient to attempt to cope with his or her deficits (43).

It has also been proposed that life events have a modulating role in the course of schizophrenic illness (23, 29), but their weight in predicting relapse probably depends to a certain extent on personal adaptive capabilities and the effectiveness of coping strategies. Patients are likely to have fewer and less flexible personal and social resources than most people with which to cope with family tension or stressful events when they arise. Thus, the role of stress in schizophrenic disorder may involve not only exposure to somewhat greater levels of stress but also limited coping resources.

In particular, complaints of hyperarousal/overstimulation in our patients were associated with a small P3b amplitude. Moreover, the availability of problem-solving coping mechanisms is a protective factor and enhances tolerance to stress. We found that subjects with a higher documented level of cognitive impairment had a higher rate of non-problem-solving coping mechanisms.

Attempts at self-protection may be more or less effective in managing the various types of internal or external strain. For instance, if certain instances of stress are long-lasting or uncontrollable, coping strategies directed at controlling these strains will probably fail and lead to further stress (44).

Our results support the hypothesis that cognitive vulnerability (both objectively documentable and subjectively experienced) enhances susceptibility to stressful events and could be considered an index for relapses, at least in a subgroup or phase of schizophrenic disorder. Cognitive disturbances should be assessed in every therapeutic project and taken into account in the pharmacological "tailoring process" in order to improve the management of the disorder. The analysis of the cognitive characteristics of experience suggests not that the attempt to venture beyond the "shadow line" is a dangerous plunge into the abyss but, rather, that it is both a realistic and productive path to follow. Our finding that more severe cognitive disturbance seems to be related to enhanced susceptibility to stressful events and less-effective coping could constitute a rationale for treating cognitive dysfunctions in schizophrenia and for attending to patients' subjective experience and coping strategies.

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