

# Emotional Reactivity to Daily Life Stress in Psychosis

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**Background:** The vulnerability-stress model of psychotic disorders describes, in essence, an interaction between personal vulnerability and environmental stressors. The present study investigated this interaction and studied emotional reactivity to daily life stress as a vulnerability marker for psychotic illness.

**Methods:** Patients with psychotic illness (n=42), their first-degree relatives (n=47), and control subjects (n=49) were studied with the Experience Sampling Method (a structured diary technique assessing thoughts, current context, and mood in daily life) to assess (1) appraised subjective stress of daily events and smaller disturbances in daily life and (2) emotional reactivity conceptualized as changes in both negative affect and positive affect.

**Results:** Multilevel regression analyses showed that an increase in subjective stress was associated with an in-

crease in negative affect and a decrease in positive affect in all groups. However, the groups differed quantitatively in their pattern of reactions to stress. Patients with psychotic illness reacted with more intense emotions to subjective appraisals of stress in daily life than control subjects. The decrease in positive affect in the relatives was similar to that of the patients, while the increase in negative affect in this group was intermediary to that of patients and control subjects.

**Conclusions:** Higher levels of familial risk for psychosis were associated with higher levels of emotional reactivity to daily life stress in a dose-response fashion. Subtle alterations in the way persons interact with their environment may constitute part of the vulnerability for psychotic illness.

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**T**HE VULNERABILITY-stress model<sup>1-3</sup> has been widely accepted as a heuristically useful framework for the study of the cause and clinical course of schizophrenia and other psychotic disorders. According to this model, psychiatric symptoms emerge whenever a threshold of stressors exceeds the individual's vulnerability level, with the latter being a stable characteristic.<sup>4</sup> The stress-vulnerability concept is essentially interactional, and as such, it remains difficult to investigate. To date, most research using this model has focussed on either the indicator of vulnerability or the stressor; whereas their interplay has rarely been examined.<sup>5</sup> For example, cognitive deficits,<sup>6</sup> abnormalities in smooth-pursuit eye movements,<sup>7</sup> alterations of event-related potentials,<sup>8</sup> and cerebral structural abnormalities<sup>9</sup> are more prevalent in the first-degree relatives of patients with schizophrenia, which suggests that they are indicators of vulnerability. Similarly, onset and relapse of schizophrenia and other psychotic disorders are associated with minor daily hassles,<sup>10</sup> life events,<sup>11,12</sup> exposure to the stresses of urban life,<sup>13</sup> or a hostile family environ-

ment.<sup>12</sup> However, these have mostly been examined without acknowledgment of their specific effects on vulnerable persons, and without acknowledging that reaction to stress is a continuous process with important intraindividual variation over time.

In the current study, we used an intensive field method<sup>14-16</sup> to examine subjective experience in the flow of daily life in order to address the following questions: (1) how does the affect of persons vulnerable to psychosis shift when they encounter a stressor in their natural environment, and (2) in what way does the emotional reaction to a real life stressor vary with differing degrees of vulnerability? Three groups were included on the basis of differences in vulnerability for psychotic illness: patients (most vulnerable), their first-degree relatives (intermediate vulnerability), and control subjects (least vulnerable).

## RESULTS

### SUBJECTS

Of the 150 subjects who entered the study, 1 control subject was excluded because of technical problems with the signalling

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## SUBJECTS AND METHODS

### SUBJECTS

The sample consisted of 50 subjects with psychotic illness (patients), 50 first-degree relatives of individuals with a psychotic illness, and 50 control subjects. All patients were receiving treatment. Selection criteria, assessed by a research physician or research psychologist, were a lifetime occurrence of psychotic symptoms (according to Research Diagnostic Criteria) for at least 2 weeks in clear consciousness for the patient group; no lifetime history of psychotic symptoms for the first-degree relatives group; and neither a family nor a personal history of psychosis, or current use of psychotropic medication for the control group. Inclusion criteria were between 18 and 55 years, sufficient command of the Dutch language, and normal physical examination results. Exclusion criteria were endocrine, cardiovascular, or brain disease; use of alcohol in excess of 5 standard units per day; weekly use of illicit drugs; and history of head injury with loss of consciousness. A fifth exclusion criterion for patients included being in need of inpatient care, intensive case management home care, or crisis intervention. Written informed consent, conforming to the local ethics committee guidelines, was obtained from all subjects. Patients were recruited through the inpatient and outpatient mental health facilities in Maastricht, the Netherlands, and through patient associations in the southern part of the Netherlands. Relatives were recruited through participating patients and relatives' groups in the same area. Control subjects were recruited from the general population in the local area through a random mailing procedure.

The diagnostic procedure included extensive screening with diagnostic interviews that included the Life Chart,<sup>17</sup> the Brief Psychiatric Rating Scale,<sup>18</sup> and the Positive and Negative Syndrome Scale,<sup>19</sup> to map psychiatric symptomatology. Interview data and clinical record data were used to complete the Operational Criteria Checklist for Psychotic Illness, yielding DSM-III-R diagnoses through the OPCRIT computer program.<sup>20</sup>

### PROCEDURE

The Experience Sampling Method (ESM) is a within-day self-assessment technique. Previous applications of ESM in patients with schizophrenia<sup>14-16</sup> have demonstrated the feasibility, validity, and reliability of the method in this population. Subjects were studied in their normal daily living environments. They each received a digital wristwatch and a set of ESM self-assessment forms collated in a booklet for each day. Ten times per day on 6 consecutive days, the watch emitted a signal (beep) at unpredictable moments between 7:30 AM and 10:30 PM. After every signal, subjects were asked to stop their activity and fill out the ESM self-assessment forms previously handed to them, collecting reports of thoughts, current context (activity, persons present, location), appraisals of the current situation, and mood. All self-assessments were rated on 7-point Likert scales.

The ESM procedure was explained to the subjects during an initial briefing session, and a practice form was completed to confirm that subjects were able to understand the 7-point Likert scale format. Subjects were instructed to complete their reports immediately after the beep, thus minimizing memory distortions, and to record the time at which they completed the form. During the actual sampling period, research staff repeatedly called the subjects to assess whether they were complying with the instructions. To know whether the subjects had completed the form within 15 minutes of the beep, the time at which subjects indicated they completed the report was compared with the actual time of the beep. All reports completed later than 15 minutes after the signal were excluded from the analysis. Previous work<sup>14</sup> has shown that reports completed after this interval are less reliable and consequently less valid. Subjects with fewer than 20 valid reports were excluded from the analysis.

### MEASURES

Mood states were assessed with 10 mood adjectives rated on 7-point Likert scales (1-7, indicating "not at all" to "very"). Factor analyses (principal component analysis with Harris-Kaiser rotation) on the raw within-subject scores identified 2 factors with eigenvalues greater than 1 explaining 41% of the total variance. Two factor-based scales with equal weights for each item were created. The mood adjectives "down," "guilty," "insecure," "lonely," and "anxious" formed the negative affect (NA) scale (Cronbach  $\alpha = .79$ ). The mood adjectives "happy," "cheerful," "relaxed," and "satisfied" formed the positive affect (PA) scale (Cronbach  $\alpha = .89$ ). The item "angry" had low loadings on both factors and was excluded to enhance differentiation between the 2 factors.

Stress was conceptualized as the subjective appraised stressfulness of distinctive events and minor disturbances that continually happen in the natural flow of daily life. Four different stress measures were computed. For event-related stress, subjects were asked to report the most important event that happened between the current and the previous reports. This event was subsequently rated on a 7-point bipolar scale (-3 = very unpleasant, 0 = neutral, 3 = very pleasant). Responses were recoded to allow high scores to reflect stress (-3 = very pleasant, 0 = neutral, 3 = very unpleasant). For activity-related stress, subjects judged their current activity on 3 self-report items (scored on 7-point Likert scales). The mean of the scales "I am not skilled to do this activity," "I would rather do something else," and "This activity requires effort," formed the activity-related stress scale ( $\alpha = .52$ ). For thought-related stress, subjects judged their thoughts at the moment of the beep on the 7-point Likert scale (ie, "My current thought is unpleasant.") For social stress, subjects were asked to evaluate the social context when other persons were present on two 7-point Likert scales "I don't like the company" and "would rather be alone" ( $\alpha = .59$ ). The mean constituted the social stress scale.

### STATISTICAL ANALYSES

Experience Sampling Method data have a hierarchical structure, and multiple observations are nested within

device (see the "Procedure" subsection). Two relatives stopped their collaboration after one day of sampling because of objections on the part of their ill relatives. Two

patients did not return the diary booklets. One family member and 6 patients were unable to comply with the research protocol (they had fewer than 20 valid reports

subjects. Initial pairwise group comparisons were performed on the subject averages for the independent and dependent variables using 1-way analysis of variance with the Tukey multiple comparison procedure. Correlations between the independent variables and the dependent variables were calculated per subject and subsequently analyzed as individual-level variables, corrected with a Fisher  $z$  transformation. One-sample 2-tailed  $t$  tests with an  $\alpha$  level of .05 were conducted to test whether the mean across people of these individual-level correlation coefficients significantly deviated from zero.

To estimate the effect of the independent variables (stress) on the dependent variables (mood), a multilevel linear random regression model<sup>21</sup> was used. Multilevel or hierarchical linear modelling techniques are a variant of the more often used unilevel linear regression analyses and are ideally suited for the analysis of ESM data consisting of multiple observations in 1 person (ie, at 2 levels [ESM-beep level and subject level]).<sup>22</sup> In the ESM, observations from the same subject are more similar than observations from different subjects; therefore, the residuals are not independent. Conventional regression techniques do not take into account the variance components at 2 different levels. Furthermore, the variance explained by autocorrelation (observations from 1 subject that are closer to each other in time will be more similar than those further apart) was taken into account by including the autoregression factor in the model.

Data were analyzed with the SAS PROC MIXED module (SAS Technical Report P-229, 1992) statistical software (SAS Institute Inc, Cary, NC). The  $\beta$  is the fixed regression coefficient of the predictor in the multilevel model and can be interpreted identically to the estimate in a unilevel linear regression analysis.

Multilevel linear regression analyses were conducted with standardized NA and PA scales as the dependent variables:

Standardized NA = NA / SD of the NA of the Whole Sample

Thus, the effect of the independent variable (stress measure) was expressed in SD units of the dependent variables (NA and PA). According to Cohen,<sup>23</sup> 0.8 SD can be considered a large effect size, and 0.2 SD, a small effect size. A group variable was constructed to reflect different levels of vulnerability for psychosis. "Group" was analyzed as a 3-level categorical variable with value labels (0 = control subjects, 1 = relatives, and 2 = patients). Group and the different stress measures, as well as their interactions (stress  $\times$  group), were the independent variables. To assess the main effects of group on mood, and to test whether the effect of stress on mood was modified by group, F tests were conducted analyzing whether the differences in intercepts and slopes were significant between the 3 categories of the group variable. The control subjects were treated as the reference group in these analyses. Analyses were conducted separately for each stress measure, followed by an analysis with all stress measures entered jointly into the model to assess the relative independence of their effects.

and were therefore excluded from the analyses, see the "Procedure" subsection). The final study sample thus consisted of 138 subjects (**Table 1**).

**Table 1. Sociodemographic and Clinical Characteristics of the Research Sample\***

Sociodemographic Variables	Subjects With Psychotic Illness (n = 42)	First-Degree Family Members (n = 47)	Control Subjects (n = 49)
Mean age, y (SD) [range]	31.9 (7.7) [20-48]	36.5 (10.7) [19-55]	35.2 (8.9) [21-50]
Male-female ratio	22:20	25:22	24:25
Education, %			
Elementary school	24	20	8
Secondary school	67	40	63
Higher education	9	40	29
Marital status, %			
Married or living together	21	68	82
Divorced	5	6	2
Never married	74	26	16
Work situation, %			
Working	24	90	98
Unemployed	0	4	2
Incapable of work	66	4	0
Protected work	10	2	0
Clinical variables			
OPCRIT <sup>20</sup> DSM III-R diagnosis (lifetime), No. of subjects			
Schizophrenia	39	0	0
Schizoaffective disorder	2	0	0
Atypical psychosis	1	0	0
Major depression	0	6	0
Mean BPRS score (SD) [range]	38 (9.8) [24-73]	28.5 (5.3) [24-51]	25.7 (2.3) [24-36]
Mean age of first psychotic episode, y (SD) [range]	22.5 (5.8) [14-41]	...	...
Usual symptom severity last 5 years (Life Chart), %			
Severe	36	...	...
Mild to moderate	57	...	...
Recovered	7	...	...
Medication status (psychotropic drugs), %			
Typical antipsychotics	50	2	0
Atypical antipsychotics	45	0	0
Antidepressants	19	4	0
Benzodiazepines	24	8	0
Lithium	5	2	0
Anticholinergics	14	0	0
No medication	5	83	100

\*Answers given as percentages indicate percentage of subjects. BPRS indicates Brief Psychiatric Rating Scale.

## STRESS AND MOOD MEASURES

Relatives and control subjects did not differ significantly on any of the 4 stress measures (**Table 2**), while patients scored significantly higher only on the event-related stress measure and the social stress measure compared with the control subjects and the relatives and control subjects, respectively. All 4 stress measures were significantly correlated within subjects, but the correlations were low. The highest mean correlation was 0.28 between the activity-related stress scale and the social stress scale (95% confidence interval [CI], 0.23 - 0.34), and the lowest mean correlation was 0.13 between the event-related stress scale and the social stress scale (95% CI, 0.09 - 0.18).

The patient group reported significantly more NA and less PA than both the relatives and the control subjects, who did not differ from each other (Table 2). The 2 dependent variables were significantly negatively correlated (mean  $r = -0.47$ ; 95% CI,  $-0.62$  to  $-0.33$ ).

## PREDICTORS OF MOOD STATES

The multilevel random regression analyses (Table 3 and Table 4) showed that the 4 stress measures were all significantly associated with mood. In addition, group was

**Table 2. Number of Valid Reports and the Independent and Dependent Variables for Patients, Relatives, and Controls\***

	Mean (SD)			$F_{2,135}$	P Value	Tukey HSD Comparisons†
	Patients (n = 42)	Relatives (n = 47)	Controls (n = 49)			
No. of valid reports	45 (10)	49 (6)	51 (5)	8.03	.001	Ps < Rs, Cs
Stress-related variables						
Event	-1.2 (0.9)	-1.3 (0.8)	-1.7 (0.7)	4.59	.01	Ps > Cs
Activity	2.5 (0.7)	2.3 (0.6)	2.4 (0.6)	0.87	.42	
Thought	3.8 (0.9)	3.6 (0.7)	3.7 (0.8)	1.02	.36	
Social	2.2 (0.8)	1.8 (0.6)	1.8 (0.6)	4.54	.01	Ps > Rs, Cs
Mood states						
Negative affect‡	1.7 (0.7)	1.3 (0.6)	1.2 (0.3)	13.49	<.001	Ps > Rs, Cs
Positive affect‡	4.4 (1)	5.2 (1.1)	5.5 (0.8)	16.32	<.001	Ps < Rs, Cs

\*For each subject, a mean was calculated over all reports, and these means were aggregated over the group to obtain the group mean (SD). HSD indicates honestly significant difference.

†Not standardized.

‡Ps indicates patients; Rs, relatives; and Cs, controls.

**Table 3. Multilevel Model Estimates for Positive Affect**

	No. of Beeps	Mean (SE) Effect of Stress on Mood* (Slope for the Entire Cohort [a])	P Value (F)	Mean (SE) Effect of Group on Mood* (Intercept Stratified by Group [b])			$F_{2,135}†$	P Value (F)
				Controls (n = 49)	Relatives (n = 47)	Patients (n = 42)		
Event-related stress	6110	-0.09 (0.01)	<.001	4.19 (0.10)	3.98 (0.10)	3.37 (0.11)	16.11	<.001
Activity-related stress	6491	-0.18 (0.01)		4.76 (0.10)	4.52 (0.10)	3.91 (0.10)	19.32	
Thought-related stress	6504	-0.11 (0.00)		4.79 (0.10)	4.54 (0.10)	3.93 (0.11)	19.00	
Social stress	4130	-0.20 (0.01)		4.73 (0.10)	4.51 (0.10)	3.93 (0.11)	16.32	

\*Based on the bivariate model: mood =  $\beta_0 + \beta_1$  stress +  $\beta_2$  group + residuals. a =  $\beta_1$ ; b =  $\beta_0 + \beta_2$  for each group.

†Based on the previous model including the interaction term  $\beta_3$  stress  $\times$  group. c =  $(\beta_1 + \beta_3) \times$  stress for each group.

‡F test for main effect of group and the stress  $\times$  group interaction term. x = 5967 for event-related stress, x = 6348 for activity-related stress, x = 6361 for thought-related stress, and x = 3988 for social stress.

§Indicates whether the differences in slope between relatives (Rs) vs controls (Cs) or patients (Ps) vs controls is significant. The controls were treated as the reference group.

||The smaller number of beeps for social stress reflects the fact that social stress was only reported when subjects were in the presence of other people.

**Table 4. Multilevel Model Estimates for Negative Affect**

	No. of Beeps	Mean (SE) Effect of Stress on Mood* (Slope for the Entire Cohort [a])	P Value (F)	Mean (SE) Effect of Group on Mood* (Intercept Stratified by Group [b])			$F_{2,135}†$	P Value (F)
				Controls (n = 49)	Relatives (n = 47)	Patients (n = 42)		
Event-related stress	6110	0.06 (0.01)	<.001	1.76 (0.11)	1.98 (0.11)	2.56 (0.12)	12.94	<.001
Activity-related stress	6491	0.11 (0.01)		1.40 (0.11)	1.64 (0.11)	2.23 (0.12)	14.91	
Thought-related stress	6504	0.05 (0.00)		1.46 (0.11)	1.71 (0.11)	2.30 (0.12)	14.26	
Social stress	4130	0.0 (0.01)		1.46 (0.10)	1.70 (0.10)	2.17 (0.11)	12.17	

\*Based on the bivariate model: mood =  $\beta_0 + \beta_1$  stress +  $\beta_2$  group + residuals. a =  $\beta_1$ ; b =  $\beta_0 + \beta_2$  for each group.

†Based on the previous model including the interaction term  $\beta_3$  stress  $\times$  group. c =  $(\beta_1 + \beta_3) \times$  stress for each group.

‡F test for main effect of group and the stress  $\times$  group interaction term. x = 5967 for event-related stress, x = 6348 for activity-related stress, x = 6361 for thought-related stress, and x = 3988 for social stress.

§Indicates whether the differences in slope between relatives (Rs) vs controls (Cs) or patients (Ps) vs controls is significant. The controls were treated as the reference group.

||The smaller number of beeps for social stress reflects the fact that social stress was only reported when subjects were in the presence of other people.

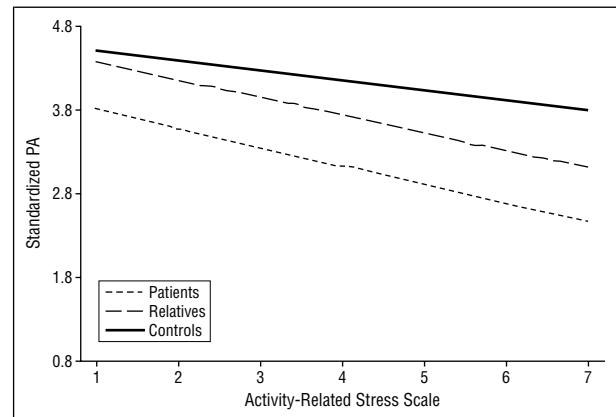
also significantly associated with both PA and NA. In agreement with the unilevel analysis in Table 2, the relatives did not differ significantly from the control subjects in prediction of mood, while the patients scored significantly higher on NA and lower on PA than the control subjects in the multilevel model (results not shown).

Significant interaction effects were found between group and all 4 stress measures for both NA and PA, indicating that the level of underlying vulnerability modified the emotional reaction toward the different stressors. For example, the effect of activity-related stress on PA was  $-0.22$  for the patient group, meaning that 1 unit of change in activity-related stress resulted in a decrease in PA of 0.22 SD. The difference between the extremes of the scales (from 1-7 on the 7-point Likert scale), therefore, was  $(6 \times 0.22)$  1.32 SDs. In the same model, 1 unit of change in activity-related stress resulted in a  $-0.21$  SD decrease in PA for the relatives group and a  $-0.12$  SD decrease for the control group. This is depicted in the **Figure**, where the predicted values of PA for each group are calculated according to the formula:

$$PA = \text{Intercept} + \text{Slope}$$

for each of the 7 levels of activity-related stress. The 2 vulnerable groups (patients and relatives) reported a

similar decrease in PA that was associated with stress (nearly parallel lines), and both were significantly larger compared with the decrease reported by the control subjects. For NA, the relatives showed a significantly greater increase in relation to stress than the control subjects, except for the social stress scale. The patients reported an even larger increase in NA compared with the con-



Effect of activity-related stress on positive affect (PA) in the 3 groups (patients, relatives, controls), as derived from the statistical model.

Mean (SE) Effect of Stress on Mood, Stratified by Group†  
(Slope Stratified by Group [c])

Controls (n = 49)	Relatives (n = 47)	Patients (n = 42)	F <sub>2,x</sub> ‡	P Value (F)	P Value (Rs vs Ps)§	P Value (Cs vs Ps)§
-0.06 (0.01)	-0.11 (0.01)	-0.11 (0.01)	8.6	<.01	<.001	<.001
-0.12 (0.01)	-0.21 (0.01)	-0.22 (0.0)	19.3	<.001	<.001	<.001
-0.08 (0.01)	-0.15 (0.01)	-0.15 (0.01)	37.78	<.001	<.001	<.001
-0.14 (0.02)	-0.25 (0.02)	-0.21 (0.03)	8.82	<.001	<.001	<.01

Mean (SE) Effect of Stress on Mood, Stratified by Group†  
(Slope Stratified by Group [c])

Controls (n = 49)	Relatives (n = 47)	Patients (n = 42)	F <sub>2,x</sub> ‡	P Value (F)	P Value (Rs vs Ps)§	P Value (Cs vs Ps)§
0.02 (0.01)	0.06 (0.01)	0.11 (0.01)	24.60	<.001	<.001	<.001
0.05 (0.01)	0.09 (0.01)	0.22 (0.01)	43.15	<.001	<.01	<.001
0.01 (0.01)	0.05 (0.01)	0.12 (0.01)	46.96	<.001	<.001	<.001
0.06 (0.02)	0.10 (0.02)	0.14 (0.02)	3.35	<.05	<.05	<.01



**Table 5. Multilevel Multivariate Model Estimates for Positive and Negative Affect\***

Effect of Stress (Stratified by Group)	Mean (SE) Positive Affect (No. of Beeps = 3645)						
	Controls (n = 49)	Relatives (n = 47)	Patients (n = 42)	P Value (Rs vs Ps)†	P Value (Cs vs Ps)†	F <sub>2,3496</sub>	P Value (F)
Effect of event-related stress	-0.04 (0.01)	-0.07 (0.01)	-0.07 (0.01)	<.05	<.05	3.77	<.05
Effect of activity-related stress	-0.08 (0.01)	-0.11 (0.02)	-0.14 (0.02)	...	<.01	3.87	<.02
Effect of thought-related stress	-0.06 (0.01)	-0.10 (0.01)	-0.12 (0.01)	<.001	<.001	11.77	<.001
Effect of social stress	-0.11 (0.02)	-0.17 (0.02)	-0.12 (0.02)	<.05	...	2.83	.06

\*Based on the multivariate model: mood =  $\beta_0$  +  $\beta_1$  event-related stress +  $\beta_2$  activity-related stress +  $\beta_3$  thought-related stress +  $\beta_4$  social stress +  $\beta_5$  group +  $\beta_6$  event-related stress  $\times$  group +  $\beta_7$  activity-related stress  $\times$  group +  $\beta_8$  thought related stress  $\times$  group +  $\beta_9$  social stress  $\times$  group + residuals. F tests were conducted to test for stress  $\times$  group interaction. Ellipses indicate not applicable.

†Indicates whether the differences in slope between relatives (Rs) and controls (Cs) or patients (Ps) and controls is significant.

control subjects. Thus, the effects of stress on NA varied in a dose-response fashion with group; the higher the degree of vulnerability, the bigger the increase in NA in response to stress.

The regression analyses with all stress measures entered together in the model showed that all measures remained significant predictors of mood. To determine which stress measure differentiated best between the 3 groups in its effect on mood, the interaction effects were added to the model (**Table 5**). Thought-related stress and event-related stress differentiated best between the 3 groups.

In a final analysis, sex was included as a possible confounder in the multivariate multilevel regression model. No significant effect of sex (0=female, 1= male) was found for either NA ( $\beta$ [SE] = .002[.088];  $P$  = .98) or PA ( $\beta$  [SE] = -.21[.15];  $P$  = .15), and the estimated effects of the stress measures differed only by a very small amount.

#### COMMENT

The results show an overall association between the subjective appraisals of events and small disturbances in the natural flow of daily life and concurrent mood. The effect sizes were small but not negligible, especially since we assessed frequently occurring exposures in daily life, the cumulative effects of which may be considerable. These results extend the results reported in several studies investigating the effects of daily events on mood<sup>24-28</sup>; specifically, the increase in perceived stress was related to an increase in NA and a decrease in PA.

Although the 4 stress measures were all independent predictors of mood (in most analyses), we would not argue, for reasons of parsimony, for separate vulnerabilities related to specific stressors. As the 4 stress measures are weakly but significantly correlated, there may be a generalized sensitivity to stress, which can be expressed in different ways.

Can stress reactivity, as defined in the present study, be considered a marker of vulnerability for psychosis?<sup>29</sup> Patients with psychotic illness deviated in emotional stress reactivity from general population control subjects. The increased stress reactivity was not likely owing solely to present psychopathology, as none of the patients was in a florid psychotic state during the ESM period (as evidenced by the low scores on the Brief Psychiatric Rating Scale), and all were *in remission*, defined as not in need

of intensive inpatient or outpatient care. Nor was it solely due to past or residual psychopathology, as the healthy relatives group also reported excess stress reactivity compared with the control group. For NA, the degree of stress reactivity paralleled the level of genetic vulnerability, with relatives showing values that were intermediate to those of patients and control subjects. For PA, an equal decrease was found for patients and relatives. Positive affect may be a less sensitive outcome to gauge subtle differences between patients and relatives. Taken together, the results suggest that stress reactivity may be considered as a behavioral expression of familial risk, and thus possibly qualify as a vulnerability marker for psychotic illness.

The differences in stress reactivity, however, might also be understood in terms of environmental and social circumstances differentially serving as risk factors or protective factors in the 3 subject groups. It has been reported that a lack of social support is associated with more emotional reactivity toward daily stressors.<sup>24,30</sup> As reduced social competence and social withdrawal are key characteristics of schizophrenia, it seems self-evident that patients with psychotic illness lack social support. The same could be true for the relatives group, as it has been reported that relatives of patients with schizophrenia more often display schizophrenialike or schizotypal traits,<sup>31</sup> such as social anhedonia (an indifference to other people),<sup>32</sup> social dysfunction,<sup>31</sup> and interpersonal problems (eg, lack of close friends).<sup>33</sup> Another explanation is that differences in stress appraisal and coping might mediate the effects of stress on mood.<sup>34</sup> Appraised stress is essentially subjective and may not necessarily correspond with the objective situation. As patients with psychotic illness tend to be more sensitive to environmental stress,<sup>12,35</sup> they would more easily report higher levels of appraised stress given an objective situation. However, the present study used appraised stress as the primary independent measure, and the patients did not report much higher levels of appraised stress. Apparently, the patients were living a “normally stressful” life that was adjusted to their impairment. Coping, on the other hand, may have little effect on mood in within-day assessments,<sup>36</sup> suggesting that coping efforts have no immediate effect on mood, and therefore, not on stress reactivity. A possible alternative explanation of the results is that living with an ill family member might strongly influence stress levels and mood in relatives. In the present study, however, only

Negative Affect (No. of Beeps = 3647)

Controls (n = 49)	Relatives (n = 47)	Patients (n = 42)	P Value (Rs vs Ps)†	P Value (Cs vs Ps)†	F <sub>2,3498</sub>	P Value (F)
0.01 (0.01)	0.04 (0.01)	0.09 (0.01)	<.05	<.001	12.81	<.001
0.04 (0.02)	0.07 (0.02)	0.14 (0.02)	...	<.001	6.78	<.001
0.0 (0.01)	0.03 (0.01)	0.10 (0.01)	<.05	<.001	25.54	<.001
0.04 (0.02)	0.06 (0.02)	0.05 (0.02)	...	...	0.25	...

some family members were living with their ill relatives (n=11), and no significant differences were found between relatives and control subjects on any dependent or independent variable.

If stress reactivity is, in addition to being an indicator of familial risk, also causally related to the development of the symptoms of schizophrenia, some clinical implications would become apparent. Stress reactivity implies an emotional reaction toward daily life stress, and as such, it leaves 2 options for intervention: (1) reducing the stressfulness of the environment or (2) altering personal reactivity. The first option has successfully been applied. For example, in family intervention studies, reducing the stress in the social environment of patients<sup>37</sup> decreased the risk of relapse. Altering personal stress reactivity, on the other hand, may be more difficult. Stress reduction techniques such as physical exercise and meditation decreased symptom severity in chronic schizophrenia<sup>38</sup>; and emotional management therapy, including relaxation and distraction techniques, improved emotional well-being in chronic schizophrenia but not in early psychosis.<sup>39</sup> Cognitive-behavioral therapy for psychosis, which is aimed at reducing emotional distress caused by psychotic symptomatology,<sup>40</sup> could possibly be extended to emotional reactivity during nonpsychotic periods to prevent relapse.

The present results should be viewed in the light of several potential methodological issues. First, they are based on subjective reports. Although subjective reports may not be highly reliable (eg, all subjects may not interpret the questions identically), they can be valid. On the other hand, the validity of objective approaches should not be taken for granted.<sup>41</sup> Second, all results have been interpreted in terms of emotional reactivity toward subjective stress. The cross-sectional analysis of the data, however, makes it impossible to establish a causal relationship. Therefore, the reverse may (also) be true. A worse mood may influence the subjective appraisal of the environment. Either explanation, however, has clinical relevance. Third, the results have been interpreted as supporting the hypothesis that stress reactivity is a vulnerability marker for psychosis. However, as no psychiatric control group was included, it is possible that stress reactivity is a vulnerability marker for psychiatric disorders in general. Stress has been hypothesized to play a role in the etiology of many psychiatric disorders.<sup>42</sup> Fourth, patients showed significantly higher levels of the depen-

dent variables NA and PA. Mood levels per se could not be considered a vulnerability marker, as relatives reported the same levels of NA and PA as the control subjects. Higher levels of NA give rise to more variability, which in turn enhances the detection of stress reactivity; however, this cannot explain the increase in stress reactivity in relatives as compared with control subjects. Finally, the increased stress reactivity in the relatives group could possibly be attributed mainly to the 6 relatives with a lifetime diagnosis of major depression or to the 11 relatives who lived with a patient. Post-hoc analyses, however, showed that parameter estimates differed only slightly and remained highly statistically significant when these subjects were excluded from the analyses.

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