# Sex Differences in Emotional Reactivity to Daily Life Stress in Psychosis

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***Background:*** The expression of schizophrenia has been reported to differ between the sexes. The current study investigates whether these sex differences in clinical expression are reflected in one underlying mechanism that may be causally related to psychosis, namely increases in stress sensitivity in daily life.

***Method:*** Forty-two participants (22 men, 20 women) with Research Diagnostic Criteria–defined psychotic disorder in a state of clinical remission were studied with the Experience Sampling Method (a structured diary technique assessing current context and mood in daily life) to assess (1) appraised subjective stress related to daily events and activities and (2) emotional reactivity conceptualized as changes in both negative affect and positive affect in relation to the subjective stress. Data were collected from January 1997 to May 1999.

***Results:*** Multilevel regression analyses revealed that women reported a significantly ($p < .05$) increased emotional reactivity to daily life stress compared with men, reflected in both an increase in negative affect and a decrease in positive affect.

***Conclusion:*** These results suggest that gender differences may not be limited to the characteristics of psychosis but may also be reflected in underlying etiologic mechanisms. Furthermore, these results might strengthen the hypothesis that women are more susceptible than men to a schizoaffective expression of schizophrenia.

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The expression of schizophrenia has been reported to differ between the sexes.[1] A number of studies have found men to display more negative symptoms than women,[2–4] while women may have a higher prevalence of affective symptoms such as dysphoria, depression, and hostility.[5,6] Furthermore, there is some evidence that women experience more positive symptoms, especially persecutory delusions[7] and auditory hallucinations.[8] Men and women have been found to differ on other illness characteristics as well. There is robust evidence that the age at onset of schizophrenia is earlier in males compared with females by 3 to 5 years,[5,6,9] and women are reported to have a more favorable course of illness then men.[10]

If the clinical characteristics of the psychotic disorder differ between the sexes, the question arises whether these sex differences are reflected in underlying mechanisms that may be causally related to psychosis. One such mechanism is increased stress sensitivity. The vulnerability-stress model postulates a causal role of increased stress sensitivity in the development of psychotic symptoms.[11,12] Indeed, onset and relapse of schizophrenia and other psychotic disorders are associated with minor daily hassles,[13] life events,[14,15] exposure to the stresses of urban life,[16] or a hostile family environment.[15] In addition, it was found that patients with psychosis and their first-degree relatives are more sensitive to stress in their daily lives compared with controls.[17]

The present study will investigate whether men and women with psychosis differ in the level of underlying stress sensitivity in daily life. Given that (1) exposure to stress is associated with the occurrence of positive symptoms of psychosis, (2) psychosis onsets preceded by stress are associated with better outcome, (3) psychosis characterized by positive rather than negative symptoms is similarly associated with better outcome, and (4) female sex is associated with both an excess of positive symptoms and a better outcome of psychotic disorder,[10,18–20] we hypothesized that female patients would display higher levels of stress reactivity than their male counterparts.

## METHOD

### Subjects

The sample consisted of 50 subjects with psychotic disorder who, according to their responsible medical

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officer, were in a stable state of clinical remission, defined as (1) being in need of routine outpatient care and not in need of hospital care, intensive case management home care, or crisis intervention and (2) having, at most, moderate levels of symptomatology. All patients were under current treatment. Selection criteria, assessed by a research physician or research psychologist, were a lifetime occurrence of psychotic symptoms according to the Research Diagnostic Criteria for at least 2 weeks in clear consciousness. Inclusion criteria were (1) age 18 to 55 years, (2) sufficient command of the Dutch language, and (3) normal results from a physical examination. Exclusion criteria were (1) endocrine, cardiovascular, or brain disease; (2) use of alcohol in excess of 5 standard units per day; (3) weekly use of illicit drugs; and (4) history of head injury with loss of consciousness. Written informed consent, conforming to the local ethics committee guidelines, was obtained from all subjects. Patients were recruited through inpatient and outpatient mental health facilities in Maastricht, the Netherlands. Data were collected from January 1997 to May 1999.

The assessment procedure included extensive screening with diagnostic interviews that included the Life Chart,[21] the Brief Psychiatric Rating Scale,[22] and the Positive and Negative Syndrome Scale[23] 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.[24]

### Experience Sampling Method

The Experience Sampling Method (ESM) is a within-day self-assessment technique.[25] Subjects are studied in their normal daily living environment. They receive a digital wristwatch and a set of ESM self-assessment forms collated in a booklet for each day. Ten times a day on 6 consecutive days, the watch emits a signal (beep) at unpredictable moments between 7:30 a.m. and 10:30 p.m. After every "beep," subjects are 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 are rated on 7-point Likert scales. Previous applications of ESM in schizophrenia[17,26–28] have demonstrated the feasibility, validity, and reliability of the method in this population. Although patients with schizophrenia report fewer valid beeps (beeps recorded according to the protocol, explained below) compared with controls (e.g., patients in the current sample: mean = 45 [SD = 10] vs. controls: mean = 51 [SD = 5]), their numbers of valid beeps are still high and acceptable. Delespaul[29] has shown that most of the patients' missing data occur at moments when they are asleep. Furthermore, patients with psychosis report similar patterns of positive and negative affect[30] and similar, although intensified, patterns of stress sensitivity in daily life[17] compared with controls. These results indicate that patients with psychosis do not fill in the booklets at random, suggesting that they are capable of using the self-report questionnaires equally as well as control subjects.

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. In order 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 more than 15 minutes after the signal were excluded from the analysis. Previous work has shown that reports completed after this interval are less reliable and consequently less valid.[29] Subjects with fewer than 20 valid reports were excluded from the analysis.

### Emotional Stress Reactivity Assessment

Previously, emotional stress reactivity was conceptualized as mood reactivity to daily events and minor disturbances in daily life (see references 17 and 28). Both the mood measures and the stress measures were derived from the experience sampling reports, as described below.

***Assessment of mood.*** Mood states reported after each beep were assessed with 10 mood adjectives rated on 7-point Likert scales (1 = "not at all" to 7 = "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 items *down, guilty, insecure, lonely,* and *anxious* formed the negative affect scale (Cronbach $\alpha = .79$). The items *happy, cheerful, relaxed,* and *satisfied* formed the positive affect scale (Cronbach $\alpha = .89$). The item *angry* had low loadings on both factors and was excluded to enhance differentiation between the 2 factors.

***Assessment of stress.*** Stress was conceptualized as subjective appraised stressfulness of distinctive events as well as of minor disturbances that continually happen in the natural flow of daily life. These were:

1. Event-related stress. After each beep, subjects were asked to report the most important event that happened between the current and the previous report. This event was subsequently rated on a 7-point bipolar Likert scale (–3 = "very unpleasant," 0 = "neutral," 3 = "very pleasant").

  

**Table 1. Sociodemographic and Clinical Characteristics of the Research Sample (N = 42)**

| Characteristic | Psychotic Subjects |
|---|---|
| Sociodemographic variable | |
| Age, mean (SD), y | 31.9 (7.7); (range, 20–48) |
| Sex, M/F | 22/20 |
| Education, % | |
| Elementary school | 24 |
| Secondary school | 67 |
| Higher education | 9 |
| Marital status, % | |
| Married or living together | 21 |
| Divorced | 5 |
| Never married | 74 |
| Work situation, % | |
| Working | 24 |
| Unemployed | 0 |
| Incapable of work | 66 |
| Protected work | 10 |
| Clinical variable | |
| OPCRIT[24] DSM-III-R diagnosis (lifetime), N | |
| Schizophrenia | 39 |
| Schizoaffective disorder | 2 |
| Atypical psychosis | 1 |
| Total BPRS score, mean (SD) | 38 (9.8); (range, 24–73) |
| Age at first psychotic episode, mean (SD), y | 22.5 (5.8); (range, 14–41) |
| Usual symptom severity last 5 years (Life Chart), % | |
| Severe | 36 |
| Mild to moderate | 57 |
| Recovered | 7 |
| Medication status (psychotropics), % | |
| Typical antipsychotics | 50 |
| Atypical antipsychotics | 45 |
| Antidepressants | 19 |
| Benzodiazepines | 24 |
| Lithium | 5 |
| Anticholinergics | 14 |
| No medication | 5 |

Abbreviation: BPRS = Brief Psychiatric Rating Scale.

Responses were recoded to allow high scores to reflect stress (–3 = "very pleasant," 0 = "neutral," 3 = "very unpleasant"). Response on this item is called *event-related stress.*

2. Activity-related stress. After each beep, subjects judged their current activity on 3 self-report items (scored on 7-point Likert scales, 1 = "not at all" and 7 = "very"). The mean of the scales ("I am not skilled to do this activity," "I would rather do something else," and "This activity requires effort") forms the *activity-related stress* scale (Cronbach a = .54).

### Statistical Analyses

A multilevel linear random regression model[31] was used. Multilevel or hierarchical linear modeling 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 within one person, i.e., at 2 levels (ESM-beep level and subject level).[32] Since, in ESM, observations from the same subject are more similar than observations from different subjects, the residuals are not independent. Conventional regression techniques do not take into account the variance components at 2 different levels.

Data were analyzed with the XTREG module in STATA.[33] The B coefficient 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.

To test the hypothesis that sex modified the emotional reaction to daily life stress, multilevel linear regression analyses were conducted with negative affect and positive affect as the dependent variables. Sex (defined as male = 0, female = 1) and the 2 stress measures as well as their interactions were the independent variables: mood = B0 + B1 daily stress + B2 sex + B3 (daily stress*sex).

The interaction term (stress*sex) was of particular interest in the present study, as the main hypothesis revolved around the question of whether sex modifies emotional reactivity to daily life stress.

## RESULTS

### Subjects and Descriptive Statistics

Of the 50 subjects who entered the study, 8 subjects were excluded from the analysis due to insufficient ESM data. Two patients did not return the diary booklets, and 6 patients were unable to comply with the research protocol (they had fewer than 20 valid reports and were therefore excluded from the analyses; see the Experience Sampling Method section). The final study sample thus consisted of 42 subjects (Table 1).

Sociodemographic and clinical characteristics of the patients are summarized in Table 1, and the mean scores on the independent and dependent variables are shown in Table 2.

### Sex Differences

The multilevel random regression analyses showed a significant main effect of the 2 stress measures on negative affect (activity-related stress: B = 0.16 [SE = 0.02], p = .0001; event-related stress: B = 0.08 [SE = 0.01], p = .0001) and positive affect (activity-related stress: B = –0.28 [SE = 0.02], p = .0001; event-related stress: B = –0.14 [SE = 0.01], p = .0001). No significant main effect of sex was apparent on negative affect (B = 0.05 [SE = 0.02], NS) or positive affect (B = –0.14 [SE = 0.3], NS).

A significant increase in negative affect associated with the daily stress*sex interaction term was found for activity-related stress (B = 0.08 [SE = 0.03], p = .012). For positive affect, there was a significant decrease associated with the event-related stress*sex interaction

**Table 2. Ratings and Correlations of the Number of Valid Reports and the Independent and Dependent Variables**

| Variable | Score | | | Correlation (r) | |
|---|---|---|---|---|---|
| | Mean | (SD) | Range | Item 1 | Item 2 |
| No. of valid reports | 45 | 10 | 21 to 60 | | |
| Stress-related variables[a] | | | | | |
| Event | –1.2 | 0.9 | –3 to 3 | 1 | |
| Activity | 2.5 | 0.7 | 1 to 7 | 0.17* | 1 |
| Mood states[a] | | | | | |
| Negative affect | 1.7 | 0.7 | 1 to 7 | 1 | |
| Positive affect | 4.4 | 1.0 | 1 to 7 | –0.43* | 1 |

[a]For each subject, a mean was calculated over all reports, and these means were aggregated over the group to obtain the group mean (SD).
*$p < .001$.

**Table 3. Effect of Daily Stress on Mood, Stratified by Sex[a]**

| Stressor | Male* | Female* | Interaction Effect [M/F] (p value) |
|---|---|---|---|
| Negative affect | | | |
| Activity-related stress | 0.11 (0.02) | 0.19 (0.02) | .012 |
| Event-related stress | 0.08 (0.01) | 0.08 (0.01) | NS |
| Positive affect | | | |
| Activity-related stress | –0.22 (0.03) | –0.33 (0.03) | .007 |
| Event-related stress | –0.10 (0.02) | –0.17 (0.02) | .021 |

[a]Values are regression coefficient B (standard error) unless otherwise stated.
*Significantly affected by daily life stressors, $p < .001$.

term (B = –0.06 [SE = 0.02], p = .021) and the activity-related stress*sex interaction term (B = –0.11 [SE = 0.04], p = .007). These results are indicative of a significantly increased emotional reactivity to daily life stress in women compared with men (Table 3).

## DISCUSSION

The present study indicated that women with psychosis may react more strongly to daily life stress compared with men with psychosis. These results suggest that gender differences may not be limited to the characteristics of psychotic disorders but may also be reflected in underlying etiologic mechanisms.

Increased stress sensitivity as an underlying etiologic mechanism for psychosis should be viewed in light of the widely used vulnerability-stress model, which postulates that patients develop symptoms due to an interaction between external stress and personal vulnerability. The hypothesis of increased stress sensitivity suggests that it is not so much the stress itself but rather the way subjects react to it that makes them vulnerable to the development of symptoms. Increased stress sensitivity has been identified in patients and their first-degree relatives, which suggests that it is at least in part genetically determined.[17] The current results suggest that women are more vulnerable than men to the effects of daily life stress. A higher level of stress reactivity may reflect a higher level of vulnerability to stressors but may also be the result of higher levels of exposure to stressors in women compared with men. Several studies in the general population have demonstrated that women are exposed to more life-event and daily stressors compared with men.[34,35] A post hoc analysis in the current sample, however, showed no significant gender difference in the amount of daily stress experienced (effect of gender on activity-related stress: B = 0.01 [SE = 0.22], NS, and event-related stress: B = –0.27 [SE = 0.28], NS). Apparently, the small stressors and disturbances in daily life are equally distributed among men and women. It is very well possible, however, that women develop higher levels of stress sensitivity by a history of increased exposure to life events and possibly also higher levels of exposure to trauma. Previous research indeed has shown that higher levels of prior exposure to life events may impact the level of stress sensitivity in daily life.[27] Thus, part of the sensitivity to stress may be genetically determined, but environmental exposures may also contribute and may explain the apparent differences between male and female patients.

The current study investigated whether reported differences in illness characteristics might also be reflected in differences in underlying vulnerability. This hypothesis fits with recent work suggesting that different vulnerability substrates might contribute to the mechanisms underlying the extensive clinical heterogeneity in schizophrenia,[28] which several authors have suggested can be reduced to 2 main forms.[20,36–39] A cognitive pathway characterized by severe cognitive deficits may be associated with a more chronic form of illness characterized by high levels of negative symptoms and neurocognitive impairment, while an affective pathway characterized by increased levels of stress sensitivity may underlie an episodic, reactive, good-outcome form with higher levels of positive symptoms. The current study reported that women are more characterized by increased stress sensitivity compared with men, indicating that they are overrepresented in the affective pathway. These results correspond with the idea that men and women are susceptible to different dimensions of variation in schizophrenia. Women are suggested to be more susceptible to a schizoaffective expression with adult onset, affective symptoms, paranoid delusions, and a stronger family history of affective disorders as prime characteristics reminiscent of the illness characteristics on the affective pathway.[5–7] Castle et al.[40] have suggested that the schizoaffective expression of psychosis may actually result from a susceptibility to affective psychosis that expresses itself phenotypically as a schizophrenia-like psychosis due to the effects of environmental insults. The recent finding that increased stress sensitivity is present in patients with psychosis, bipolar disorder, and major depression also suggests an area of shared vulnerability between affective and nonaffective psychosis, especially in women, who are most

characterized by increased stress sensitivity (at least in psychosis).[41]

### Methodological Issues

The present results should be viewed in light of several methodological issues. First, the measurements of daily stress and mood are based on subjective reports. Although subjective reports are considered less reliable (e.g., do all subjects interpret or answer the questions identically?), they can be valid, whereas the validity of objective approaches should not be taken for granted.[42]

Second, emotional stress reactivity has been defined in terms of emotional reactivity toward subjective stress. The cross-sectional analyses of the data, however, make it impossible to establish a causal relationship. Therefore, the reverse might be true, in that a worse mood might influence the subjective appraisal of the environment. The overall effect, however, would still be for the individual to experience distress associated with an environmental event.

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