# Gender Differences in the Psychopathology of Emerging Psychosis

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## ABSTRACT

**Background:** Gender differences have often been found in psychopathological symptoms among chronic schizophrenia and first-episode psychosis (FEP) patients. However, many of these studies suffer from methodological problems and show inconsistent results. Furthermore, very few studies have investigated gender differences in individuals with an at-risk mental state (ARMS) for psychosis.

**Methods:** Psychopathological symptoms were assessed in 117 ARMS and 87 FEP patients by two observer-rated scales, namely, the expanded version of the Brief Psychiatric Rating Scale (BPRS) and the Scale for the Assessment of Negative Symptoms (SANS), and by one self-report scale, the Frankfurt Complaint Questionnaire (FCQ). Gender differences were investigated by applying Analyses of Variance using the BPRS, SANS and FCQ subscales as dependent variables, and group and sex as between-subject factors - in a second step by including age, antipsychotic, antidepressant and cannabis use as covariates.

**Results:** There were no significant gender × patient group interactions, suggesting that gender effects did not differ between patient groups. Women had higher scores in positive psychotic symptoms (BPRS Psychosis/Thought Disturbance) while men had higher scores in negative symptoms (BPRS negative symptoms, SANS total score, as well as subscales Affective Flattening, Avolition-Apathy and Asociality-Anhedonia). However, the differences did not withstand correction for multiple testing. The results did not change when corrected for potential confounders.

**Conclusions:** There do not seem to be any gender differences in psychopathology, neither in ARMS nor in FEP patients, as regards self-reported or observer-rated symptoms, when corrected for multiple testing and potential confounders.

## INTRODUCTION

The analysis of gender differences in schizophrenia has been of interest for many decades. Kraepelin had already observed, on the basis of medical histories of 225 men and 449 women, that the classical picture of schizophrenia with early manifestation, deficits in premorbid development, affective flattening and social anhedonia seems to occur much more often in men than in women (1). The empirical data collected since then appear to confirm this, especially the gender differences with regards to an earlier manifestation age of psychosis in men than in women (for review, see 2, 3-5). Many studies have also reported that men have poorer premorbid adjustment and present with more negative, but fewer depressive symptoms than women (for review, see 6, 7, 8). Furthermore, women seem to have a better response to antipsychotics than men (9, 10).

However, the problem of many studies conducted in this area is that frequently the examined populations were neither representative, nor restricted to first contact patients or first admissions, or important covariates were not considered (11-13). Furthermore, the diagnostic concept applied is important. Thus, Addington et al. (14), in a study on 113 inpatients meeting DSM-III-R criteria

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for schizophrenia, reported that gender differences in negative and affective symptoms disappear when the sample is restricted to narrowly defined schizophrenia.

Empirical studies that were clearly restricted to first episode psychosis (FEP) patients are rather inconclusive. Thus, for instance Szymanski et al. (15) reported more anxiety, illogical thinking, inappropriate affect, and bizarre behavior in women than in men. No gender differences in FEP were found in Barajas et al. (16). Häfner et al. (4), who carried out a representative study of all 276 first hospitalized FEP patients from a well-defined catchment area with a population of about 1.5 million inhabitants in and around Mannheim, Germany, did not find many gender differences. Especially with respect to psychotic symptoms after correction for multiple testing, no statistically significant gender differences were found anymore. They rather found differences in illness behavior with more self-neglect and cannabis abuse in men and more over-adaptive behavior in women (17, 18). These authors noted that methodological problems (see above), but possibly also the higher prevalence of substance abuse in men, could have contributed to gender differences found in other studies (19).

More recent studies investigating gender differences regarding symptoms in clearly representative samples of first episode patients were conducted by Salokangas and Stengård (20), Thorup et al. (21), Koster et al. (22), Cotton et al. (23) and Bertani et al. (24). The most commonly reported findings in these studies were more negative, but less affective symptoms, poorer social functioning and more social isolation in men than in women (20, 21, 24, 25) and also more substance abuse in men (21, 23, 25).

There are only few studies about psychopathological gender differences in individuals with a so-called at-risk mental state for psychosis (ARMS). All of these reported no gender differences regarding symptoms at baseline (26-28). When baseline and follow-up time points were considered collectively, Willhite et al. (26) found significantly higher levels of negative symptoms and marginally lower levels of social functioning in men.

To our knowledge, the present study is the first to investigate gender differences in psychopathology in a largely representative sample of both ARMS individuals and FEP patients, considering important potential confounders such as age, duration of untreated illness (DUI), antipsychotic and antidepressant medication, and cannabis use. The goal of the study was to elucidate whether gender differences in psychopathology in fact do exist in ARMS or FEP, in order to provide clinical evidence to improve the early detection of psychosis. We hypothesized that the gender differences in psychopathology in ARMS and FEP found in some of the previous studies could be explained by potential confounders such as higher substance use in men compared to women.

## MATERIAL AND METHODS

### SETTING AND STUDY POPULATION

Participants were recruited via the Früherkennung von Psychosen (FePsy) Clinic, a specialized clinic for the early detection of psychosis at the Department of Psychiatry, University Hospital in Basel, Switzerland, from March 1, 2000, to September 1, 2012. The present study is a part of an ongoing study on the early detection of psychosis. The ARMS and FEP groups were identified using the Basel Screening Instrument for Psychosis (BSIP), a 46-item instrument based on variables that have shown to be risk factors and early indicators of psychosis (29). This instrument allows the rating of individuals with beginning psychosis in the atypical early stages of the disease with a good reliability and validity (29, 30) according to the criteria of Yung and co-workers (31).

### INCLUSION CRITERIA

Subjects were included as ARMS individuals if they met the following inclusion criteria based on our screening instrument (29) and the Brief Psychiatric Rating Scale (BPRS) (version Lukoff et al. [32] and Ventura et al. [33]):

i. Prepsychotic category (according to Yung et al. [31] and BPRS version/scale Lukoff et al. [32]). "Attenuated" psychotic symptoms: psychotic symptoms below transition cut-off (BPRS scales: hallucinations 2–3, unusual thought content 3–4, suspiciousness 3–4) at least several times per week, in total persisting for >1 week; or Brief Limited Intermittent Psychotic Symptoms (BLIPS): psychotic symptoms above transition cut-off (BPRS scales: hallucinations ≥4, unusual thought content ≥5, suspiciousness ≥5, conceptual disorganisation ≥5), but each symptom <1 week before resolving spontaneously.
ii. Genetic risk category: first or second degree relative with psychotic disorder and at least two further risk factors according to screening instrument.
iii. Unspecific risk category: minimal amount and combination of certain risk factors according to screening instrument.

Precondition for all categories: criteria of transition to psychosis not fulfilled.

Criteria i) and ii) correspond to those of Yung et al. (31). Criterion iii) additionally permits the inclusion of individuals at lower risk, i.e., of patients without pre-psychotic symptoms or genetic risk who only exhibit a combination of certain unspecific risk factors and indicators such as prodromal symptoms or marked social decline (unspecific risk group).

#### TRANSITION CRITERIA

Inclusion criteria for FEP patients and criteria for transition to psychosis: FEP patients were those who at intake already fulfilled the criteria for transition to psychosis as defined by Yung et al. (31):

- At least one of the following symptoms: Suspiciousness (BPRS ≥5): says others are talking about him/her maliciously, have negative intentions or may harm him/her (incidents more than once a week OR partly delusional conviction). Unusual thought content (BPRS ≥5): full delusion(s) with some preoccupation OR some areas of functioning disrupted (not only ideas of reference/persecution, unusual beliefs or bizarre ideas without fixed delusional conviction). Hallucinations (BPRS ≥4): occasional hallucinations or visual illusions >2/week or with functional impairment (not only hearing of own name, non-verbal acoustic or formless visual hallucinations/illusions). Conceptual disorganization (BPRS ≥5): speech difficult to understand due to circumstantiality, tangentiality, neologisms, blockings or topic shifts (most of the time OR three to five instances of incoherent phrases).
- Symptoms at least several times a week.
- Change in mental state lasting >1 week.

The patients were only included in the study if they had not received antipsychotic treatment for more than a maximum of three weeks.

If the patients fulfilled the inclusion criteria, they were asked to participate in the FePsy study, an open, prospective clinical study on the early recognition of schizophrenic psychosis.

#### EXCLUSION CRITERIA

Exclusion criteria were age <18 years, insufficient knowledge of German, IQ <70, psychosis clearly due to organic brain disease or substance abuse (except cannabis), psychotic symptomatology within a clearly diagnosed affective psychosis or borderline personality disorder, or lifetime antipsychotic treatment for more than a maximum of three weeks (total chlorpromazine equivalent dose ≥2500 mg) (34).

More detailed descriptions of the study design, recruitment and inclusion criteria have been provided elsewhere (30, 34). All aspects of the study were approved by the Ethics Committee of Basel (EKBB), Switzerland, and written informed consent was obtained from each study participant.

#### CLINICAL DATA AND PSYCHOPATHOLOGICAL ASSESSMENT

At the time of study inclusion, psychopathological symptoms were assessed with the expanded version of the Brief Psychiatric Rating Scale (BPRS) (32, 33), the Scale for the Assessment of Negative Symptoms (SANS) (35) and the Frankfurt Complaint Questionnaire (FCQ) (36). The BPRS consists of 24 items and is one of the most frequently used research instruments for evaluating psychopathological symptoms in patients with schizophrenia (37). Although there is no widely accepted factorial structure of the BPRS, several authors have proposed a four factorial structure. In the present study, we used the BPRS total score and the four subscales (i.e., Depression/Anxiety, Psychosis/Thought Disturbance, Negative Symptoms, and Activation) derived from the factorial structure of Velligan et al. (37), as their study was based on the largest sample size.

The SANS is a well-recognised rating scale for the assessment of negative symptoms in schizophrenia. It consists of 19 items, which are grouped into five domains or factors (Affective Flattening, Alogia, Avolition-Apathy, Anhedonia-Asociality, and Inattention). In the present study, we used the SANS total score and the five original subscales.

The FCQ is a self-rating scale that is composed of 98 yes/no questions. It is one of the most widely used procedures for systematic investigation of non-psychotic subjective experiences (i.e., so-called basic symptoms) in emerging psychoses and has been adapted to several languages (38). Basic symptoms are subjective subclinical disturbances in avolition, affect, thought, speech, perception and stress tolerance, which can occur at every stage of psychotic disorders, in ARMS individuals, in prodromes of relapse, and during psychotic episodes (39). FCQ items are grouped into ten categories according to phenomenological similarities. Exploratory factor analyses, however, suggest only 2-4 underlying factors (40). In this study, we used the four scales derived from the factorial structure of Süllwold and Huber (41) (i.e., Disturbances of automated responses, Perceptual disturbances, Depression and Overinclusion) and the FCQ total scale.

The duration of untreated illness (DUI) was defined as the time period between first self-perceived signs or symptoms and first contact with our specialized early

detection clinic. The duration of untreated psychosis (DUP) was defined as the time period between the appearance of first psychotic symptoms and first contact with our FePsy Clinic. The DUI and DUP were determined by using the Basel Interview for Psychosis (BIP) ) (42), a structured and specifically developed interview for the early detection of psychosis. The DUI was assessed both for ARMS and FEP patients at first contact, but the DUP was only assessed in FEP patients since ARMS patients per definition did not have psychotic symptoms yet.

## DATA ANALYSIS

All data were analyzed by using SPSS for Windows (version 19). Univariate differences in socio-demographic and clinical characteristics between male and female patients within each patient group (i.e., ARMS, FEP, and combined group) were tested with t-tests, Mann-Whitney U tests, $\chi 2$ and Fisher's exact tests. These tests were two-tailed with a significance level of 0.05.

Multivariate differences in psychopathology were investigated by applying a one-way analysis of variance (ANOVA) for each of the 16 clinical variables (i.e., 5 BPRS scales, 6 SANS scales and 5 FCQ scales). The clinical variables served as the dependent variables, and gender and patient groups (ARMS or FEP) were included as between-subject factors. In case of a significant group by gender interaction, ANOVAs were followed up by subgroup analyses. Moreover, to investigate whether gender differences were biased by confounding variables, age, DUI, use of antipsychotic, antidepressant and cannabis were introduced into the models in a stepwise manner. Specifically, cannabis use was included in the multiple regression models as a categorical variable represented by four dummy variables. Due to the large number of comparisons, p-values of the gender effects in the ANOVA models were corrected by the Benjamini-Hochberg method that controls for the false discovery rate (43).

## RESULTS

### SAMPLE CHARACTERISTICS

Of the ARMS and FEP patients recruited into FePsy study, in 117 ARMS (men/women 1.72) and 87 FEP patients (male/female 1.81) at least one of the analysed rating scales was completed. The BPRS ratings were obtained in 114 ARMS and 86 FEP patients, the SANS ratings in 110 ARMS and 81 FEP patients, and the FCQ was completed in 69 ARMS and 55 FEP patients.

Demographic and clinical characteristics of the ARMS, FEP and total groups are presented in Table 1. No statistically significant univariate differences were found between men and women with regard to age, years of education, cannabis use, antipsychotic and antidepressant use, neither within the total sample nor within the FEP and ARMS groups.

The DUP and the DUI did not differ between male and female ARMS and FEP patients, and within the total group. Furthermore, there were no statistically significant DUI × gender × group interactions.

### GENDER DIFFERENCES IN PSYCHOPATHOLOGY

Table 1 also shows the univariate comparisons of the BPRS, SANS and FCQ subscales between men and women within each patient group. Mean scores and 95% confidence intervals of these psychopathological symptom scales within ARMS and FEP patients are additionally presented in Figure 1.

When uncorrected for multiple testing, within the total group men had higher scores than women in the BPRS subscale "negative symptoms", in the SANS total score as well as the SANS subscales "Affective Flattening," "Alogia" and "Asociality-Anhedonia," Within the ARMS group, women had significantly higher scores than men in the BPRS subscale "Depression/Anxiety," whereas men had higher scores than women in the SANS total score as well as the SANS subscales "Alogia" and "Asociality-Anhedonia. Within the FEP group, higher scores in the BPRS subscale "negative symptoms" were found in men compared to women.

In multivariate analyses, there were no statistically significant gender × group interactions for any of the 16 dependent variables. Hence, all multivariate analyses were performed in the total group only. Regression coefficients, uncorrected p-values and p-values corrected by Benjamini-Hochberg adjustment for multiple testing are shown in Table 2. Negative values of the regression coefficients mean that women had lower scores on the assessed scales. The main effect of gender was significant for the BPRS subscales "Psychosis/Thought disturbance" and "Negative symptoms", in the SANS total score as well as the SANS subscales "Affective Flattening, "Avolition-Apathy" and "Asociality-Anhedonia. This means that women had more positive psychotic symptoms and thought disturbances, but fewer negative symptoms than men and that there were no gender differences in other domains such as affective symptomatology (see Table 2). However, these differences were no longer significant when p-values were corrected for multiple

**Table 1.** *Socio-demographic and clinical characteristics of ARMS and FEP patients*

| | All | | | | ARMS | | | | FEP | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Women N=74 | Men N=130 | p-value | N | Women N=43 | Men N=74 | p-value | N | Women N=31 | Men N=56 | p-value | N |
| Age | 28.1(9.8) | 26.8(6.8) | 0.301 | 204 | 26.7(9.5) | 25.3(6.4) | 0.395 | 117 | 30.1(9.9) | 28.7(6.9) | 0.508 | 87 |
| Years of education | 11.4(3.0) | 11.4(3.1) | 0.904 | 204 | 11.8(3.1) | 11.8(3.2) | 0.943 | 117 | 10.9(2.9) | 11.0(3.1) | 0.888 | 87 |
| DUP [months] | | | | | | | | | 25.4(39.7) | 47.9(74.5) | 0.106 | 69 |
| DUI [months] | 56.8(68.2) | 54.7(63.9) | 0.848 | 150 | 67.9(73.7) | 51.0(55.1) | 0.264 | 85 | 39.5(56.0) | 58.9(73.5) | 0.244 | 65 |
| Current cannabis use | | | 0.089 | 204 | | | 0.244 | 117 | | | 0.207 | 87 |
| None | 58(78.4%) | 80(61.5%) | | | 35(81.4%) | 50(67.6%) | | | 23(74.2%) | 30(53.6%) | | |
| Rarely | 3(4.1%) | 11(8.5%) | | | 1(2.3%) | 3(4.1%) | | | 2(6.5%) | 8(14.3%) | | |
| Several times per month | 3(4.1%) | 3(2.3%) | | | 2(4.7%) | 2(2.7%) | | | 1(3.2%) | 1(1.8%) | | |
| Several times per week | 4(5.4%) | 15(11.5%) | | | 1(2.3%) | 10(13.5%) | | | 3(9.7%) | 5(8.9%) | | |
| Daily | 6(8.1%) | 21(16.2%) | | | 4(9.3%) | 9(12.2%) | | | 2(6.5%) | 12(21.4%) | | |
| Antipsychotics currently | | | 0.542 | 204 | | | 0.133 | 117 | | | 0.962 | 87 |
| No | 65(87.8) | 119(91.5%) | | | 41(95.3%) | 74(100%) | | | 24(77.4%) | 45(80.4%) | | |
| Yes | 9(12.2%) | 11(8.5%) | | | 2(4.7%) | 0(0.0%) | | | 7(22.6%) | 11(19.6%) | | |
| Antidepressants currently | | | 1.000 | 204 | | | 1.000 | 117 | | | 1.000 | 87 |
| No | 61(82.4%) | 106(81.5%) | | | 34(79.1%) | 58(78.4%) | | | 27(87.1%) | 48(85.7%) | | |
| Yes | 13(17.6%) | 24(18.5%) | | | 9(20.9%) | 16(21.6%) | | | 4(12.9%) | 8(14.3%) | | |
| BPRS Depression/Anxiety | 2.6(1.0) | 2.4(1.0) | 0.252 | 199 | 2.6(0.9) | 2.2(0.9) | 0.034* | 113 | 2.6(1.0) | 2.7(1.1) | 0.646 | 86 |
| BPRS Psychosis/Thought Disturbance | 2.3(1.0) | 2.1(0.9) | 0.145 | 201 | 1.8(0.7) | 1.6(0.6) | 0.229 | 115 | 3.1(0.9) | 2.8(0.9) | 0.139 | 86 |
| BPRS Negative symptoms | 1.8(0.9) | 2.1(1.0) | 0.011* | 200 | 1.8(0.9) | 2.1(1.0) | 0.123 | 114 | 1.7(0.8) | 2.1(1.0) | 0.033* | 86 |
| BPRS Activation | 1.6(0.7) | 1.5(0.7) | 0.494 | 200 | 1.4(0.7) | 1.4(0.5) | 0.768 | 114 | 1.9(0.7) | 1.7(0.8) | 0.473 | 86 |
| BPRS total score | 1.9(0.5) | 1.9(0.5) | 0.731 | 200 | 1.7(0.5) | 1.7(0.4) | 0.573 | 114 | 2.2(0.5) | 2.2(0.5) | 0.989 | 86 |
| SANS Affective Flattening | 0.7(1.0) | 1.0(1.0) | 0.039* | 189 | 0.7(1.1) | 1.1(1.0) | 0.120 | 108 | 0.7(0.9) | 1.0(1.1) | 0.176 | 81 |
| SANS Alogia | 0.6(0.8) | 0.9(1.1) | 0.035* | 189 | 0.6(0.8) | 0.9(1.0) | 0.049* | 109 | 0.7(0.8) | 0.9(1.1) | 0.359 | 80 |
| SANS Avolition-Apathy | 1.7(1.2) | 2.0(1.0) | 0.051 | 191 | 1.7(1.0) | 1.9(1.0) | 0.214 | 110 | 1.7(1.4) | 2.2(1.1) | 0.141 | 81 |
| SANS Asociality-Anhedonia | 1.7(1.4) | 2.2(1.3) | 0.011* | 186 | 1.7(1.4) | 2.3(1.3) | 0.049* | 106 | 1.7(1.3) | 2.1(1.3) | 0.110 | 80 |
| SANS Inattention | 0.9(1.2) | 1.2(1.2) | 0.178 | 172 | 0.8(1.0) | 1.1(1.1) | 0.166 | 97 | 1.1(1.5) | 1.3(1.3) | 0.545 | 75 |
| SANS total score | 1.0(0.8) | 1.4(0.9) | 0.006* | 191 | 1.0(0.8) | 1.4(0.9) | 0.027* | 110 | 1.1(0.8) | 1.4(0.9) | 0.109 | 81 |
| FCQ Disturbances of automated responses | 0.3(0.3) | 0.3(0.3) | 0.694 | 124 | 0.3(0.2) | 0.3(0.2) | 0.826 | 69 | 0.4(0.3) | 0.4(0.3) | 0.792 | 55 |
| FCQ Perceptual disturbances | 0.2(0.2) | 0.2(0.2) | 0.984 | 125 | 0.1(0.1) | 0.1(0.1) | 0.492 | 70 | 0.2(0.2) | 0.3(0.3) | 0.621 | 55 |
| FCQ Depression | 0.4(0.2) | 0.4(0.3) | 0.841 | 125 | 0.3(0.2) | 0.3(0.2) | 0.668 | 70 | 0.4(0.2) | 0.4(0.3) | 0.845 | 55 |
| FCQ Overinclusion | 0.4(0.2) | 04(0.3) | 0.339 | 124 | 0.4(0.2) | 0.3(0.2) | 0.195 | 69 | 0.5(0.2) | 0.5(0.3) | 0.968 | 55 |
| FCQ total score | 0.3(0.2) | 0.3(0.2) | 0.704 | 124 | 0.3(0.2) | 0.2(0.2) | 0.521 | 69 | 0.4(0.2) | 0.4(0.3) | 0.909 | 55 |

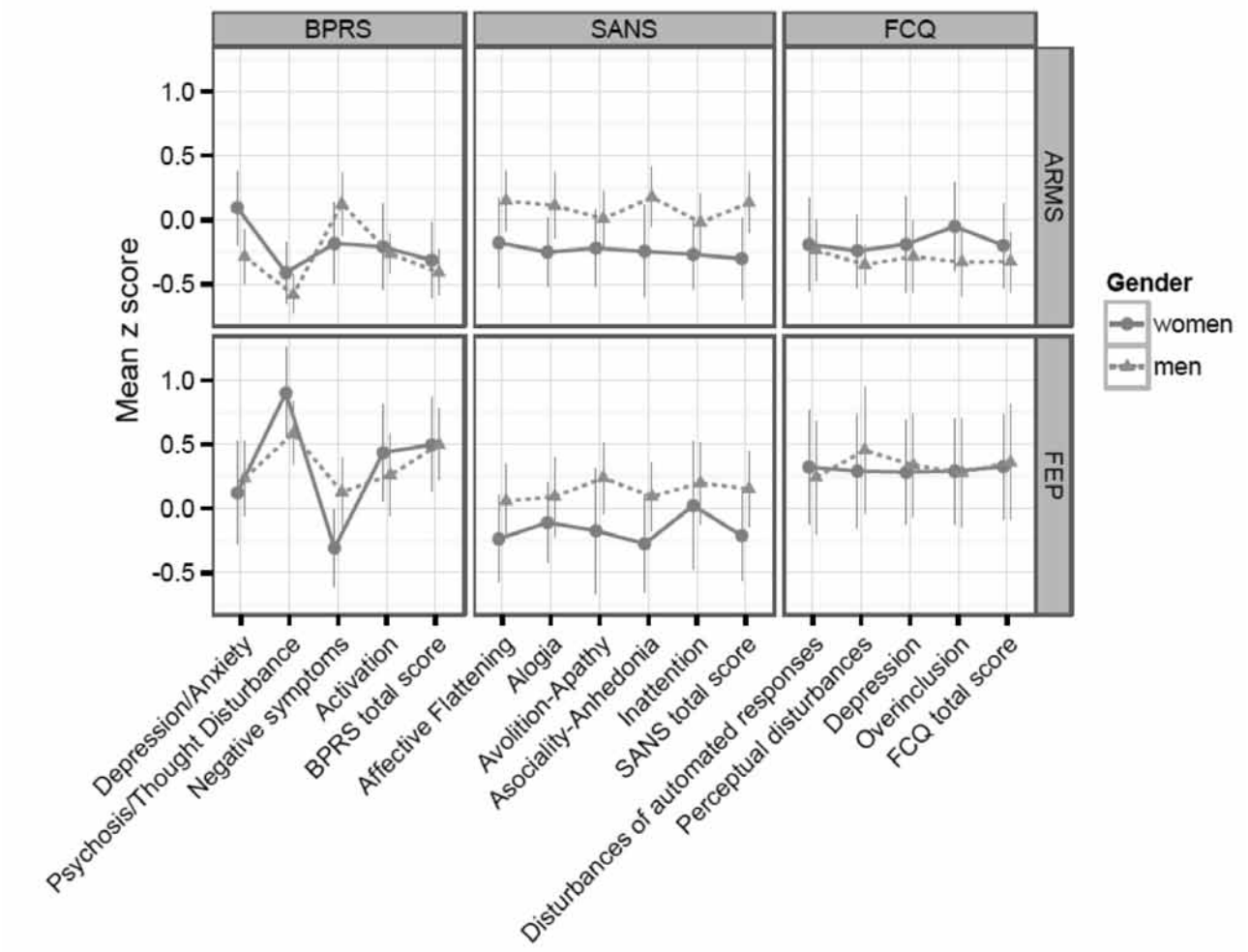
*P<0.05
ARMS= At-risk mental state; FEP= First episode of psychosis; DUP= Duration of untreated psychosis; DUI= Duration of untreated illness; BPRS= Brief Psychiatric Rating Scale; SANS= Scale for the Assessment of Negative symptoms; FCQ= Frankfurt Complaint Questionnaire. Values of continuous variables are given as means with standard deviations in parentheses.

testing by using the Benjamini-Hochberg adjustment (see Table 2). Furthermore, the results did not change when age, DUI, cannabis use, antipsychotic and antidepressant use were included into the models as covariates.

## DISCUSSION

The aim of this study was to investigate gender differences in psychopathology in a sample of 117 ARMS individu-

**Fig. 1.** *Symptomology in At-Risk Mental State and First Episode Psychosis Patients in the FePsy-Study*
*Means and 95% confidence intervals of subscales of the Brief Psychiatric Rating Scale (BPRS), Scale for the Assessment of Negative Symptoms (SANS) and Frankfurt Complaint Questionnaire (FCQ) within the groups of at-risk mental state (ARMS) and first episode psychosis (FEP) patients. All scales were z-transformed based on means and standard deviations of the total group. Women N = 74; Men N = 130.*




als and 87 FEP patients. We conducted a cross-sectional analysis as part of the FePsy study (34), an open longitudinal prospective and observational study, which aims to improve the early detection of psychosis. We examined the hypothesis that gender is associated with different psychopathological patterns in at-risk mental states for psychosis and at the first onset of psychosis. In a further step, we included potentially confounding factors such as age, duration of untreated illness, cannabis use, antipsychotic and antidepressant use.

As regards potentially influencing factors of psychopathology, no statistically significant gender differences were found regarding age at the time of study inclusion, years of education, antipsychotic and antidepressant use, neither within the total sample nor within the FEP and ARMS groups. Within the ARMS group, our findings are in line with previous studies (26, 44) that found no significant gender differences in demographic factors and psychiatric medication intake. Within the FEP group, our results on demographic features are supported by recent findings by Bertani and colleagues (24) who carried out the PICOS study, a representative study of all FEP patients from a catchment area of nearly 3.3 million inhabitants in northeastern Italy. These authors found no statistically significant differences in educational levels between male and female FEP patients.

In our study, a tendency to gender differences regarding cannabis use was shown. Within the ARMS and FEP groups, men had higher cannabis use rates compared to women. This finding is in line with the above mentioned

**Table2.** *Symptomatology in AtRisk Mental State and First Episode Psychosis Patients - multiple regression models with gender, patient group, cannabis use (categorical) and gender × group interaction.*

| | Coefficient[1] | p-value (uncorrected) | p-value (corrected by BH adj.[2]) |
|---|---|---|---|
| BPRS Depression/Anxiety | 0.065 | 0.382 | 0.634 |
| BPRS Psychosis/Thought Disturbance | 0.104 | 0.082 | 0.195 |
| BPRS Negative symptoms | -0.188 | 0.010** | 0.103 |
| BPRS Activation | 0.042 | 0.420 | 0.634 |
| BPRS total score | 0.009 | 0.817 | 0.873 |
| SANS Affective Flattening | -0.171 | 0.038* | 0.151 |
| SANS Alogia | -0.136 | 0.084 | 0.195 |
| SANS Avolition-Apathy | -0.148 | 0.085 | 0.195 |
| SANS Asociality-Anhedonia | -0.245 | 0.019* | 0.103 |
| SANS Inattention | -0.123 | 0.219 | 0.438 |
| SANS total score | -0.170 | 0.014* | 0.103 |
| FCQ Disturbances of automated responses | 0.013 | 0.610 | 0.813 |
| FCQ Perceptual disturbances | -0.004 | 0.795 | 0.873 |
| FCQ Depression | 0.000 | 0.984 | 0.984 |
| FCQ Overinclusion | 0.019 | 0.436 | 0.634 |
| FCQ total score | 0.004 | 0.819 | 0.873 |

ARMS women: N = 43; ARMS men: N = 74; FEP women: N = 31; FEP men: N = 56; Total N = 204
*p<0.05; **p<0.001
[1]Negative values of the regression coefficients mean that women had lower scores on the assessed scales.
[2]BH adj= Benjamini-Hochberg adjustment for multiple testing.

ABC study that found higher substance abuse in men than women in the early phases of psychoses (4, 19).

There were no statistically significant DUI or DUP and gender × group interactions in our study. For this reason, gender differences in psychopathology do not seem to be influenced by the duration of untreated illness or psychosis in our ARMS and FEP samples. These findings are consistent with the PICOS study (24), which reported that DUP did not differ significantly by gender and had no confounding effect on psychopathological symptoms in FEP patients.

As regards psychopathology in our study, when uncorrected for influencing factors and multiple testing, we found that male ARMS individuals had significantly higher negative symptom scores, whereas women had higher scores in depressive symptoms. Also within the FEP group, men were more likely to present negative symptoms than women. Despite this tendency, statistically significant differences in psychopathological symptoms could not be confirmed between men and women, in both ARMS individuals and FEP patients, when p-values were corrected for multiple testing. Within the ARMS group, these findings are in agreement with Willhite and colleagues (26) who found no significant gender differences in ratings of any of the symptoms of the Scale of Prodromal Symptoms (SOPS) (45) at baseline. Within the FEP group, this is in agreement with the most representative study carried out by Häfner et al. (12), and a recent systematic review (8), which reported no gender differences in psychopathological symptoms in emerging psychoses. Also in the ABC study (19), prior to the correction for Type I error, male FEP patients had shown higher scores in loss of interest, self-neglect, slow speech, obsessional thoughts, alcohol and drug abuse. Women were more likely to present delusions of guilt and incongruity of affect. However, these gender differences were no longer present when p-values were adjusted for multiple testing (12), similar to what was shown in our study. Furthermore, Bertani et al. (24) found no significant gender differences in psychopathology assessed by the PANSS scale and subscales (positive, negative and general subscales) in FEP patients.

Our findings on gender differences in psychopathology did not change when age, duration of untreated illness (DUI), cannabis use, antidepressant and antipsychotic use were included into the models as covariates. These findings are consistent with Bertani et al. (24) who controlled gender differences in FEP patients for age.

To the best of our knowledge, this is the first study to examine gender differences in psychopathology concomitantly in both ARMS and FEP patients by using both observer-rated scales and a self-report scale, and including age, DUI, cannabis, antidepressant and antipsychotic use as potential confounders together.

So far there are only few studies on gender differences in psychopathology of ARMS individuals and results of studies investigating FEP patients are inconsistent. This might be due to several reasons. Methodological differences between studies such as different study designs, and a lack of a systematic and homogenous assessment of psychopathological symptoms could have contributed to the inconsistencies. Many studies have recruited patients from chronic populations, inpatient units or private clinics, that cannot be considered a representative population of a catchment area. Furthermore, the sample sizes in many studies were small. Häfner et al. (4) were the first

to specifically control selection and diagnostic bias in the ABC study. Patients included in our study also seem to be fairly representative for our catchment area as our early detection clinic FePsy is the only one in our area.

A further strength of our study is that we investigated gender differences in psychopathological symptoms with two well established observer-rated scales (BPRS and SANS) (32, 35) and a self-report scale (FCQ) (36). A limitation is that the FCQ scale could not be obtained in half of the patients, which limited the statistical power.

In conclusion, the present study could not confirm significant gender differences in psychopathology in ARMS individuals or FEP patients. Nevertheless, further studies to examine gender differences in ARMS and FEP patients in larger populations controlling for important confounding factors such as age, medication and cannabis use are warranted.

## CONTRIBUTIONS

Alexandre González-Rodríguez was involved in the analysis and interpretation of data, and wrote the first draft of the manuscript. Erich Studerus supported statistical analyses and reviewed the paper. Charlotte Rapp, Andrea Spitz, Hilal Bugra, Jacqueline Aston and Stefan Borgwardt critically revised the manuscript. Anita Riecher-Rössler designed the study, supervised the whole project and revised the paper.

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