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Sex versus gender differences in schizophrenia: The case for normal personality differences

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ABSTRACT

Schizophrenia has generally been viewed as having a unique preschizophrenia personality or destructive to the personality post-onset. This view is reflected in the scarcity of studies of personality in schizophrenia with the exception of schizotypal personality considered by many as an endophenotype of schizophrenia. What is missing is the study of personality as independent of schizophrenia and as a potential source of schizophrenia heterogeneity. In this study we examine sex versus gender as an initial effort to introduce personality as a normal variant that influences how schizophrenia is expressed. Gender, a personality construct, was associated with the presence of depression in a large sample of schizophrenia patients controlling for sex, age of onset, severity of disorder, and education. The results suggest that gender, rather than sex, as a representative personality trait may yield important insights into how schizophrenia is expressed.

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1. Introduction

As recently pointed out by Silverstein et al. (2014) "... despite thousands of new studies every year, and major technological advances, schizophrenia research is not leading to consistent improvements in the lives of people with the disorder" (p. 259). One of the obstacles identified in trying to advance treatment is within schizophrenia heterogeneity, a phenomenon that has plagued the study, understanding, and treatment of schizophrenia since the time of Kraepelin and Bleuler. Numerous efforts over three decades have been made to understand this variability within schizophrenia; these include the study of sociodemographic characteristics, subtypes, premorbid competence, genetic risk, familial environment, and brain morphology (Corvin et al., 2013; Johnston, 1992; Silveira et al., 2012). We suggest in this study the use of personality differences, using gender as an exemplar and proof of concept, to address some of the variability in the clinical expression in schizophrenia.

The study of personality in schizophrenia has exclusively focused on between-diagnosis comparisons in the pursuit of identifying diagnostic markers, with the assumption that there are shared personality characteristics in schizophrenia (Berenbaum and Fujita, 1994; Ohi et al., 2016). There is a strong bias, introduced by Kraepelin and Bleuler, that the prepsychosis personalities of schizophrenia patients are different from those with other disorders or healthy individuals. In a meta-analysis of the then-current research, Berenbaum and Fujita (1994) went so far as to ignore the absence of statistical significance in their findings to

interpret the data as supporting personality differences in pre-schizophrenia individuals. Current research, while more rigorous in adhering to statistical guidelines, continues to focus on the "unique" personality characteristics of schizophrenia (Ohi et al., 2016).

The study of sex differences in schizophrenia has yielded promising findings, largely in the realm of timing of disorder as a function of neurohormonal processes (e.g. Abel et al., 2010; Goldstein and Lewine, 2000; Salem and Kring, 1998). With rare exceptions, however, "sex" and "gender" have been conflated both in the use of language and in conceptualization. Specifically, although personality may be embedded in the biology of the individual (see Canli, 2006), sex and gender are not the same. It has been more than two decades since Deaux (1993) called for clarification of the two terms. She argued that sex refers to the genetic features that identify man or woman, while gender incorporates aspects of personality, namely more masculine or more feminine, that can apply to either or both of the sexes. The personality framework of gender (semi-independent of sex) is exemplified in the work of Bem and the identification of androgynous, as well as feminine and masculine types across the sexes (Bem, 1994). Importantly, subsets of both men and women were classified as masculine, feminine, and androgynous. With respect to research strategies, Deaux (1993) captured this type of separation between sex and gender in pointing to the differences between "sex comparisons" [woman to man and girl to boy] and "gender comparisons" [gender identification, gender stereotypes, and gender roles]. The two types of comparisons can yield different results and may have different implications, a perspective we explore in understanding schizophrenia.

The purpose of this study was to contrast sex and gender differences in schizophrenia, viewing gender as a personality characteristic. In

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general, there are multiple confirmed “sex differences”, ranging across biological, psychological, and social domains and include age of onset of the disorder, incidence and prevalence of psychosis, risk factors, symptom expression and outcome (Abel et al., 2010; Falkenburg and Tracy, 2012; Goldstein and Lewine, 2000; Nasser et al., 2002). Briefly, the data suggest that men with schizophrenia have an earlier onset of psychosis, greater social impairments, more negative symptoms, poorer neuropsychological functioning, and poorer outcomes than women with schizophrenia. The focus of this study is the symptomatic expression of affect. Specifically, women are more likely than men to exhibit affect, in particular negative affect such as depression and anxiety, than are men. All of the studies reported in published reviews of sex differences used self-identified sex (woman/man comparisons) as the independent variable, although just as often as not using the term “gender” to refer to the man–woman categorization. In short, none of these studies distinguished between sex and gender, thereby overlooking potential sex, gender (personality), or sex by gender interactions.

As we reported earlier (Lewine, 1991, 2004), consideration of sex and gender separately yielded provocative findings in a large sample of schizophrenia patients. Although among those with schizophrenia, women tended to do better than men on tests of neuropsychological functioning, feminine (as measured by the MMPI mf scale) of both sexes performed better than masculine individuals of both sexes. The current study examined the separate impacts of sex and gender on the clinical expression of schizophrenia, with a particular focus on depression for which there is a well-established sex difference. If sex and gender are, indeed, not synonymous with one another, we would expect them to have different relationships with well-established “sex” differences or to account for what appear to be sex differences. A better understanding of personality characteristics (measured as gender in this study), in contrast to sex, could have significant implications for our diagnosis, treatment, and understanding of schizophrenia.

2. Methods

2.1. Participants

The data used in this study were collected as part of a larger study of sex differences in schizophrenia (details available from the first author). The data from 213 participants (141 men and 72 women) were used in this study. The majority of patients were diagnosed with schizophrenia ($n = 170$) and the remainder with schizoaffective disorder ($n = 43$). As expected, a significantly larger proportion of women (33.3%) than men (13.5%) received the diagnosis of schizoaffective disorder (Fisher's Exact Test, $p = 0.002$). A summary of participant demographic characteristics is provided in Table 1. Participants met the diagnostic criteria of schizophrenia according to the DSM-III-R. Trained clinicians conducted semi-structured interviews and completed clinical ratings; the patients completed self-report questionnaires, including the MMPI.

Table 1
Means (s.d.) of demographic characteristics of patients by sex and gender.

	Women		Men	
	Feminine	Masculine	Feminine	Masculine
Age at MMPI	37.9 (11.8)	36.6 (19.7)	34.06 (10.2)	31.6 (8.2)
Race (% white)	80.6	50.0	87.6	72.2
AFH	24.7 (10.3)	26.1 (9.6)	21.9 (6.2)	21.6 (7.2)
Education (Years)	13.2 (2.7)	11.5 (1.5)	13.25 (2.3)	11.9 (1.9)
Duration (Years)	12.9 (8.4)	10.5 (13.7)	12.1 (9.5)	9.9 (6.7)

Note: MMPI = Minnesota Multiphasic Personality Inventory; AFH = age of first hospitalization.

Age MMPI: Sex, $F_{1, 209} = 4.253, p = 0.04$.

AFH: Sex, $F_{1, 207} = 5.639, p = 0.018$.

Education: Gender, $F_{1, 206} = 10.464, p = 0.001$.

2.2. Measures

2.2.1. Gender-MMPI

We used the MMPI mf (masculine–feminine) scale to measure gender, a strategy supported by the literature (Nasser et al., 2002). Further, the mf scale has been reported to exhibit significant overlap with the Bem Sex Role Inventory and the Personal Attributes Questionnaire, both more widely accepted gender measures (Volentine, 1981). To make gender comparable to sex assignment in this study, namely dichotomous, following Bem's strategy we generated two categories of gender: masculine and feminine. The mf scale contains a total of sixty items covering four major content areas: interests in vocations and hobbies, aesthetic and religious preferences, activity–passivity, and personal sensitivity.

High scores reflect sex-atypical characteristics. An atypical male would be passive and socially sensitive, while the atypical female would be considered aggressive and dominating. Easy going and adventurous traits would represent the typical male role, while the typical female role would be represented by more submissive and passive traits. The mf scale was used to classify men and women as sex typical or atypical (T-scores above 60 relative to large non-clinical samples), yielding four groups: “masculine” men, “feminine” men, “masculine” women, and “feminine” women.

Of the 141 men, 74.4% were classified as sex atypical (feminine) and 21.7% of the 72 women were classified as sex atypical (masculine), the distributions approaching statistical significance (Fisher's Exact Test, $p = 0.055$). The differential distribution of gender atypical by sex is consistently reported in the study of both patients and healthy individuals (Duckworth and Anderson, 1986). That is, more men (especially among more educated) score in the atypical range than do women.

2.2.2. Clinical expression

(1) MMPI- patients completed the MMPI, from which profiles were generated, excluding the mf scale; (2) Hamilton Depression Rating Scale–clinician rating of depressive symptoms; (3) Scale for Assessment of Positive Symptoms [SAPS] and Scale for Assessment of Negative Symptoms [SANS]–clinician rated positive and negative symptoms; (4) Global Assessment of Functioning [GAF]–clinician rating of patient's social, vocational, and overall functional level.

3. Results

3.1. Sociodemographic characteristics

As expected from prior analyses of these data, men were significantly younger than women at age of first hospitalization for psychosis (Table 1; $F_{1, 207} = 5.639, p = 0.018$). Masculine patients were only slightly younger at first hospitalization than feminine patients (22.6 and 22.9, respectively, ns). The interaction of sex and gender was also not statistically significant.

3.2. Clinical presentation

MMPI (Figs. 1 [Men] and 2 [Women]): We divided a conventional significance level of 0.05 by the 11 MMPI clinical scales, resulting in 0.0045 as the statistical cut point for considering significance in a MANOVA of all MMPI scales (excluding mf), using mf defined gender and self-reported sex as the independent variables. There were two highly significant main effects of Gender, in each case with feminine patients, independent of sex, scoring higher than masculine patients: depression ($F_{1, 209} = 8.678, p = 0.004$) and hysteria ($F_{1, 209} = 11.397, p = 0.001$). There were no significant sex differences and only one Sex \times Gender interaction effect on MMPI scales: masculine women and feminine men scored significantly higher than their counterparts on the F scale ($F_{1, 209} = 13.420, p < 0.0001$), often interpreted as a sign of distress; that is, within each sex, the sex atypical group reported

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