

## A sex and gender-differentiated approach in psychiatric care: is the time ripe?

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To the Editor,

Sex and gender are acknowledged as important variables in medicine. In psychiatry, although a sex and gender-differentiated diagnostics and management approach has not yet been outlined, indisputable evidence points to sex and gender variables in neuropsychiatric disorders. The prevalence, age of onset and clinical symptoms of many neuropsychiatric diseases differ substantially between males and females. Psychological factors such as women's unique attachment patterns, relational self-construction, gender-based power dynamics and the distorted division of labor play an important role in the gender difference in depression (1).

Gender identity (the self-identification with the male or female sex), sexual orientation, and the risks for neuropsychiatric disorders develop in our brain during early development.

The initial interest in gender issues was stimulated by recognition that women were almost absent from much medical research. In fact, partly due to concerns about possible teratogenic side-effects, an overwhelming majority of men were enrolled in early trials, which led to female patients undergoing drug treatments according to what had been found to work in male patients (2). Such inconsistencies and distortions resulted in reports reflecting higher rates of adverse events in women, although such drugs had been prescribed to both male and female patients.

Research perspective has included more specific attention and sensitivity to the role of gender differences. In that respect, it would also be advisable to

implement, whenever possible, a disaggregation of research findings based on sex (3), i.e. the full and thorough reporting of data identifying all relevant information for targeted research studies and meta-analyses on sex-specific trends. Similar approaches need to be gradually implemented for gender-based differentiation, which is absolutely relevant in psychiatry. Gender used to be intended as a twofold, or "binary" factor including male and female. Nowadays, however, gender has increasingly come to identify a range or spectrum of sex-related perceptions of oneself, often grouped under the term non-binary (2, 3).

In light of the above, it is advisable to work towards more sex- and gender-stratified evidence and guidelines accounting for sex/gender-specific medicine, in terms of dosage, tolerability, possible interactions and side effects, sensitivity of diagnostic tests, and distinct treatment strategies. The possible benefits of new rising technologies such as telepsychiatry, which particularly during the COVID-19 pandemic (4) has rapidly asserted itself as a valuable tool, should be maximized. The pandemic itself has highlighted the importance of more effective targeted and specific prognostic/therapeutic approaches, given the impact it has had on mental health and substance use disorders (5), whose treatment also should consider gender as a relevant element. New trafficking avenues have been shaping up with the rise of novel psychoactive substances, extremely hard to trace (6, 7) and detect but considerably harmful for public health. Biological, genetic, epigenetic, psycho-social, cultural, and environmental factors all play a synergistic role in defining sex/gender differences, in SUDs as well as mental disease overall,

and even in bringing about sex/gender inequality. Understanding such dynamics and taking stock as to the role of sex/gender in physiological and pathological processes is essential if we are to optimize prevention strategies, the identification of clinical signs, prognosis definition, and lay out more effective, tailored therapeutic pathways. Ultimately, such approaches will have to move beyond “binary” conceptions (2) and acknowledge the highly relevant role of gender identity in psychiatric care and research for the sake of mental health. Hopefully, such efforts will be instrumental in devising strategies to best help those for whom gender dysphoria and incongruence is a debilitating major issue.

**Conflict of Interest:** The author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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