II European Meeting on Women's Mental Health

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PSYCHOSIS AND GENDER

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Abstracts – Plenary Lectures

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INDEX

Plenary Lectures

Inaugural Lecture

Impact of genes on sex differences in brain development and psychosis.

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Differences between men and women with psychotic illness have been described since Kraepelin's founding of modern psychiatry at the turn of the 20th century. Notably, schizophrenia (SCZ) has 1.4-fold higher incidence in males than females, while onset is typically 5-10 years later in females than males. Further, female SCZ patients generally have less severe deficit symptoms, better response to antipsychotics, and milder cognitive deficits than male patients. Despite these well-documented sex differences in SCZ, the underlying mechanisms are essentially unknown, which hinders our understanding of the etiology of brain dysfunction in SCZ that is critical for developing better treatments.

A leading hypothesis is that sex differences in SCZ are mediated by sex differences in brain abnormalities that are laid down during early brain development. During fetal development, gonadal hormones affect the expression of genes that mediate the development of brain regions and formation of brain circuits. There is evidence that specific brain circuits are disrupted in SCZ patients in sex-dependent ways. For example, normal patterns of male/female differences in the structure of brain regions that develop during the second and third trimester of fetal development are disrupted in SCZ patients, suggesting that factors contributing to normal sexual dimorphisms underlie brain abnormalities in SCZ. While there is ample evidence that sex differences in brain anatomy, neurochemistry, and behavior in SCZ are mediated by hormone and genetic effects primarily acting during fetal development, few studies have investigated how changes in these genes might influence this process.

Indeed, genes play a large role in susceptibility to common neurodevelopmental and psychiatric disorders, including SCZ, which has a relatively high estimated heritability of 60-80%. Studies of family transmission patterns in the 1980's and '90's found differences in the prevalence of SCZ in relatives of male compared to female patients, suggesting that genes may have different effects on SCZ risk in males and females.
A recent, large-scale genome-wide association study (GWAS) identified 108 chromosomal loci associated with SCZ risk across males and females, including 3 loci on the X chromosome that could feasibly contribute to sex differences in SCZ risk. Interestingly, many of the genes in the 108 loci are more highly expressed in fetal brain compared to later developmental stages through late adulthood, suggesting that SCZ risk genes are enriched for genes operating during fetal brain development when sexual dimorphism emerges.

Previous candidate gene association studies and GWAS have reported sex-specific associations (occur on only one sex) or sex-dependent associations (quantitatively different effects in males and females). However, these prior studies are relatively small and a systematic investigation of genetic influences on sex differences in SCZ has not been performed. We are currently addressing this gap by leveraging large patient GWAS datasets assembled by the Psychiatric Genomics Consortium to identify genetic loci that contribute to sex differences in SCZ susceptibility. We are performing association analyses of

genetic variants that interact with sex to confer disease risk (i.e., sex-by-gene interactions). We hypothesize that genetic variation contributes to SCZ by disrupting the healthy sexual dimorphism of the brain, resulting in differential effects in female and male SCZ patients on the development and function of brain circuits underlying this disorder. These studies are expected to provide new leads on genetic origins of sex differences that lie at the core of SCZ pathology.

Plenary Lecture

Schizophrenia in the perinatal period.

Prof. Louise Howard. Institute of Psychiatry, Psychology and Neuroscience at King's College London. South London and Maudsley NHS Foundation Trust. United Kingdom.

Although women with schizophrenia have reduced fertility most will experience pregnancy. These pregnancies are complex as they are at increased risk of obstetric and psychiatric complications, and are associated with multiple comorbid problems and women face stigma and discrimination. This lecture will provide an overview of recent evidence on the care of women with schizophrenia in the perinatal period; although schizophrenia is a perinatal mental disorder with a limited evidence base, optimal management could prevent adverse outcomes for the mother with schizophrenia and her family.

Plenary Lecture

Gender aspects in psychosis high-risk states and first episode patients

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Objective: To review sex and gender differences in emerging psychoses, i.e. the prodromal phase of psychosis and its first episode (FEP).

Methods: Literature review and presentation of own data from the Basel ***FePsy*** (***F***rüh***e***rkennung von ***Psy***chosen; early detection of psychoses) study, a long-term follow-up study of individuals with an at-risk metal state (ARMS).

Results: As a literature review showed, studies on gender differences in ARMS and FEP s how inconsistent findings, mainly due to methodological problems and discrepancies of studies, which will be discussed.

In our FePsy study we only found very few gender differences regarding psychopathology. However, duration of untreated psychosis was significantly shorter in women, and they more often had a partner whom they approached for help. Also, regarding neurocognition there were only very few gender differences, which were similar to those found in healthy controls. There were no significant differences regarding transition rates. Interestingly, there were sex differences regarding psychoendocrinology with women having a higher rate of hyperprolactinemia and increased pituitary volumes.

Conclusions: Overall, only few gender differences in individuals with emerging psychosis, ARMS and FEP seem to exist, which very much resemble the gender differences found in the general population. This implies that gender differences in emerging psychosis, if there are any, are not disease-specific but more due to general differences between men and women.