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Abstracts – Symposiums

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Symposiums

Symposium 1: *Gender differences in emerging psychosis*

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Symposium Abstract

Background: Gender differences in schizophrenic psychoses have often been reported. However, little is known about gender differences in the very early stages of the emerging disorders.

Information: This symposium summarizes empirical evidence from three studies focusing on gender differences in emerging psychosis.

Goals: This symposium tries to address these open questions.

Importance: The clinical and research relevance of focusing on sex and gender differences in first episode of psychosis (FEP) and at-risk mental state (ARMS) patients should be emphasized.

Summary: Data from a general population sample aged 8 to 40 years of the canton of Berne, Switzerland, will be presented regarding the question of gender-specific peculiarities. Results will be presented assessing gender differences in prevalence of ultra-high risk (UHR) symptoms, in different age groups and gender effects in the association between UHR symptoms and both psychosocial functioning and axis I disorders.

While sex differences in schizophrenia are well documented, findings in the so-called at-risk mental state (ARMS) for psychosis and in first episode psychosis (FEP) are scarce. Especially in the field of neuroanatomical studies sex differences have largely been neglected. This talk will give an overview about the current state of literature and ongoing studies investigating sex differences in emerging psychosis. Recent findings and implications for future research will be discussed.

Finally, one of the first long-term follow-up studies of ARMS patients will be presented, focusing not only on late transitions and its potential predictors but also on remission and protective factors, including gender and its associated factors. The hypothesis of women showing a better course with more remissions and better psychosocial functioning will be tested.

Speakers' Abstracts

Gender specific peculiarities in the prevalence of ultra-high-risk symptoms- results from a general population study

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Objectives: In the early detection of psychosis, developmental and gender specific peculiarities are often neglected. Therefore, the aim of the present study was to (i) examine gender differences in prevalence of ultra-high-risk (UHR) symptoms in different age groups and (ii) to examine gender effects in the association between UHR symptoms and both psychosocial functioning and axis-I disorders.

Methods: The sample comprised 1486 (736 females; 49.5%=) individuals aged 8-40 years from the general population of Canton Bern, Switzerland, enrolled in either of two studies from June 2011 until March 2016. Perceptive and non-perceptive attenuated psychotic symptoms (APS) and brief intermittent psychotic symptoms (BIPS) as well as the respective UHR criteria (incl. onset/worsening and frequency requirements) were assessed using the Structured Interview for Psychosis-Risk Syndromes.

Results: Compared to males, females showed a significant higher prevalence of APS (16.4% versus 10.4%), of UHR criteria (1.2% versus 0.4%) and of any axis-I disorder (18.7% versus 9.9%). A gender-specific impact of age was only found for perceptive APS: Compared to the reference group of 20-24-year-olds, girls aged 8-19 years (OR=3.9; CI: 2.0-7.5) as well as boys aged 8-12 years reported more perceptive APS (OR=5.0; CI: 1.9-13.0). No interaction of gender and UHR symptoms was found to affect psychosocial functioning and axis-I disorders.

Conclusion: The higher prevalence of UHR symptoms in females and the age-gender interaction for perceptive, but not non-perceptive APS highlights the importance of considering both gender and age in the early detection. Longitudinal studies should address the impact of these findings on prediction of psychosis.

Sex differences in brain morphology in emerging psychosis

Laura Egloff

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Objective: Early detection of schizophrenic psychoses based on clinical signs is a promising approach to prevent a poor outcome in patients with a so-called at-risk mental state (ARMS) for psychosis. However, it is not yet possible to reach sufficient accuracy in the prediction of transition to psychosis. For one, this may be due to the different disease trajectories male and female patients experience. While sex differences in schizophrenia are well documented, research on sex differences in ARMS patients is scarce. In the field of neuroanatomical

studies normal sexual dimorphism of healthy people has been shown to be disrupted in schizophrenia. As alterations of the brain structure can be explanations for some sex differences in these disorders, it is crucial to explore when these alterations occur. We have therefore examined if disrupted or even reversed sexual dimorphism is already present in the at-risk mental state (ARMS) for psychosis and in first episode psychosis (FEP) patients.

Methods: Data were collected within the prospective FePsy (Früherkennung von Psychosen; early detection of psychoses) study. Structural T1-weighted images of 65 ARMS (73.8% male; age = 25.1 ± 6.32) and 50 FEP (74% male; age = 27 ± 6.56) patients were compared to those of 70 healthy controls (HC; 38.6% male; age = 26 ± 4.97). All images were acquired using a 3 Tesla magnetic resonance imaging scanner. For ease of interpretation of the brain structural volumes 1) the cube root was taken, 2) volumes were normalized to the individual whole brain volume by dividing them by the total brain volume, 3) volumes were centred and scaled (i.e., z-transformed). By applying linear mixed effects models we investigated whether subcortical brain volumes are dependent on sex.

Results: We found men to have larger total brain volumes ($p < .001$), and smaller bilateral caudate ($p = .008$) and hippocampus volumes ($p < .001$) than women across all three groups. Older subjects had significantly more gray matter and white matter volumes than younger subjects. No significant sex × group interaction was found.

Our results point towards still existing patterns of normal sexual dimorphism in total brain and caudate volumes in emerging psychosis. The only structure affected by reversed sexual dimorphism was the hippocampus, with women showing larger volumes than men even in HC. Hence, subcortical volumes may not be primarily affected by disrupted sexual dimorphism in emerging psychosis.

Discussion/Conclusion: In times of growing interest in personally tailored interventions in medicine and health care, most of our knowledge about psychoses and schizophrenia stems from research in male subjects and may therefore not fully apply to females. Thus, sex and gender are increasingly being acknowledged as important determinants and essential aspects of research in the field of mental and physical health.

Investigations of sex-specific brain structural and functional alterations and their associations with pathophysiology are needed to improve our understanding of the aetiopathogenesis of schizophrenic psychoses and the treatment of the disorder.

Gender differences in the long-term course of at-risk mental state individuals

Katharina Beck

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Objectives: Gender differences have been extensively studied in schizophrenia patients with the most consistently shown results being higher age of onset and better prognosis in women. So far, only few studies have evaluated gender differences in individuals with an at-risk mental state (ARMS) for psychosis far. Findings were mostly inconsistent, although some studies reported increased negative symptoms and poorer psychosocial functioning in men. The aim of our study was to investigate differences between male and female ARMS individuals in regard to long-term clinical course, functional outcome and protective factors.

Methods: We conducted long-term follow-up assessments in ARMS individuals that were initially included in the FePsy (Früherkennung von Psychosen; early detection of psychoses) study and the Bruderholz study, and did not transition to frank psychosis during the initial follow-up periods of these research projects. In the FePsy study, patients were recruited between 2000 and 2014 and initially followed for up to 5 years, whereas in the Bruderholz study, patients were recruited between 2004 and 2006 and initially followed for up to 2 years. The long-term assessments took place from 09/2015 to 02/2017, up to 15 years after baseline. Remission from the ARMS was defined as the absence of attenuated psychotic symptoms or brief limited intermittent psychotic symptoms for at least 12 consecutive
months preceding the long-term follow-up examination. Outcomes of interest were remission from ARMS, clinical symptoms (PANSS), diagnoses (DSM-IV; SCID-I), psychosocial functioning (GAF, Personal and Social Performance Scale; PSP) and potential protective factors, i.e., resilience (Resilience Scale for Adults; RSA) and coping strategies (Structured interview for the assessment of coping with schizophrenia - subscale "self-efficacy"; IKB).

Results: There were no gender differences in regard to remission from the ARMS as well as in regard to positive, negative and general symptoms or functional outcome. Considering the whole follow-up period, more women had episodes of mood disorders. Rates of anxiety disorders, alcohol dependence and substance use disorders did not differ. Men and women did not differ regarding functional outcome. Concerning resilience, there was a trend towards better social resources and a more structured approach towards daily living in women. Help- seeking as a coping strategy was more prevalent in women, and there was a tendency to more active coping in women, while both genders reported the same amount of avoidance as
coping mechanism.

Conclusions: This is one of the first studies to evaluate gender differences in long-term outcome and protective factors of ARMS individuals. Male and female ARMS individuals did not differ in regard to long-term clinical and functional outcome except for a higher prevalence of mood disorders in women, which is in line with epidemiological research. Additionally, our findings suggest a trend towards increased resilience and better help- seeking and active coping in women. The consideration of gender differences in psychopathology and coping behavior in ARMS individuals in clinical practice could further improve outcome of both men and women.

Symposium 2: *Psychosis and gender: Do reproductive phases matter?.*

Moderator: Gemma García-Parés. Mental Health Service. Hospital Nostra Senyora de Meritxell. Andorra.

Symposium Abstract

The present symposium will review the relationship between the reproductive phases and the effects of sexual steroids on mental Health, mainly in psychoses. The first speaker, Dr Pirec will focus in postpartum and perimenopause symptoms of anxiety, depression and psychoses and she will present two cases that exemplifies these conditions.

The second speaker, Dr Usall, will present data about the efficacy of raloxifene , a selective estrogen receptor modulator, as an adjuvant treatment for postmenopausal women with schizophrenia. She will focus mainly in the results of two clinical trials conducted by her research team.

Speakers

- ***Postpartum anxiety gradually progressing into psychosis: case presentation and theoretical prospective.***
  Vesna Pirec. ERC Insight in Chicago. University of Illinois at Chicago. Rush University Medical School. USA.

- ***Raloxifene as an adjunctive treatment for postmenopausal women with schizophrenia.***
  Judith Usall. Parc Sanitari Sant Joan de Déu. CIBERSAM. Barcelona. Spain.

Symposium 3: *Sex, hormones and clinical outcome of psychotic disorders: roles for cortisol, prolactin and estadiol.*

Moderator: Javier Labad. Department of Mental Health. Corporació Sanitària Parc Taulí. Sabadell. Spain.

Symposium Abstract

BACKGROUND

Stress and hormones are thought to play a role in the pathogenesis and outcome of psychotic disorders. Recent evidence suggests that there might be sex-differences in the association between stress-related hormones (prolactin, cortisol) and sex steroids in relation to the pathogenesis and clinical outcome of early psychosis.

GOALS

The present symposium will address whether there are sex differences in psychoneuroendocrinological aspects of early psychosis with a particular focus on hypothalamic-pituitary-adrenal axis hormones, prolactin and estradiol. It will also address potential effects of prolactin in the outcome of psychotic disorders, including cognitive impairment and sexual dysfunction.

IMPORTANCE

The knowledge of the existence of sex-specific associations between hormonal measures and the clinical phenotype of early psychotic subjects will be of great interest for both clinicians and researchers in the field of psychosis. This symposium will also address the role of hyperprolactinaemia on sexual dysfunction, an important cause of poor treatment adherence in patients with a psychotic disorder.

SUMMARY

INTRODUCTION: Research suggests abnormalities in hypothalamic-pituitary-adrenal (HPA) axis function play an important role in the pathophysiology of psychosis. Recent studies also suggest a potential role for other hormones including prolactin and sex steroids. Hyperprolactinaemia is a common condition in patients with a psychotic disorder that can induce sexual dysfunction. There is limited research exploring whether there are sex-differences in these psychoneuroendocrinological issues.
OBJECTIVES: To address whether there are sex-differences in the relationship between hormones and the pathogenesis and outcome of early psychosis.
METHODS AND RESULTS: Data will be presented by means of revision of the literature as well as by bringing preliminary data from research teams interested in the study of psychoneuroendocrinological aspects of early psychosis. Studied populations will include both young people at ultra-high-risk (UHR)

for psychosis and first episode psychosis. Hormonal measures will include dynamic HPA-axis tests in saliva (cortisol awakening response) and plasma levels of hormones (cortisol, prolactin and estradiol). Clinical outcomes will include the risk of psychosis transition, symptom severity of psychotic and depressive symptoms, cognitive functioning and sexual dysfunction. The results of different studies suggest that sex is an important variable in the relationship between hormones and the clinical phenotype of early psychosis. These results stress the importance of considering sex differences in the psychosis-risk period, as they improve understanding of pathogenic processes. The contribution of hyperprolactinaemia to the presence of sexual dysfunction underscores the need to monitor this side effect in patients receiving antipsychotic treatment.

Speakers

- ***Sex, stress and the hypothalamic-pituitary-adrenal axis in early psychosis.***
  Javier Labad. Department of Mental Health. Corporació Sanitària Parc Taulí. Sabadell. Spain.

- ***A possible role for prolactin and estradiol in emerging psychosis.***
  Sarah Ittig. Center for Gender Research and Early Detection, University of Basel Psychiatric Hospital. Switzerland.

- ***Sex-differences in the relationship between prolactin levels and impaired processing speed in early psychosis.***
  Itziar Montalvo. Department of Mental Health. Corporació Sanitària Parc Taulí. Sabadell. Spain.

- ***Anti-psychotic induced hyperprolactinaemia and its role in sexual dysfunction.***
  Elena Rubio-Abadal. Parc Sanitari Sant Joan de Déu. CIBERSAM. Barcelona. Spain.

Symposium 4: *New Perspectives on the biology and risk of Postpartum Psychosis.*

Moderator: Narcis Cardoner. Corporació Sanitària Parc Tauli. Chairman of Societat Catalana Psiquiatria i Salut Mental. Sabadell. Spain.

Symposium Abstract

Postpartum psychosis (PP) is the most severe psychiatric disorder associated with childbirth affecting 1-2 in every 1000 women, typically occurring in the first 6 weeks after delivery and it is highly predictable: in fact, around 35% of women with a history of bipolar affective disorder or with a previous history of PP, will suffer PP after giving birth. Although PP occurs in concomitance with the biological changes of childbirth, its neurobiological basis is still poorly understood, partially as a consequence of lack of studies looking at biological factors and having no amenable animal models.

Dr Andrew Lawrence and Dr Montserrat Fusté will present results from a pilot and prospective study looking at women at risk of PP. Their talks will be focused on brain structural abnormalities and peripheral gene expression profiling changes among women at risk of PP. Dr William Davies and collaborators suggested that maternal deficiency for the enzyme steroid sulfatase may predispose to PP, his group have recently shown that inhibition of the STS enzyme in new mouse mothers is associated with abnormal behavioural phenotypes that can be alleviated by antipsychotic administration.

Dr Andrew Lawrence will discuss whether women who develop a PP episode differ in structural brain abnormalities in brain cortical volume and morphology from women who are at risk of PP but do not develop PP episodes, and from women without mental illness in the same postpartum period. Dr Montserrat Fusté is going to show gene expression profiling, immune inflammatory and metabolic pathways that distinguish those at risk but remain well, those that develop PP and healthy controls. Dr Davies will show gene expression analyses in this new pharmacological mouse model with the aim to identify abnormally-functioning molecular pathways that underlie PP risk.

Despite the fact that PP is one of the most severe psychiatric disorders, and the time of maximum risk is identifiable, there has been little research attempting to characterize the biology and the prediction of postpartum psychosis. Therefore, preclinical and clinical studies are needed to identify biological markers for PP.

This symposium offers new perspectives on PP, revealing findings related to brain structure and immune-endocrine gene expression alterations known to be relevant to psychosis.

Speakers

- **Novel findings in brain structure in women at risk of Postpartum Psychosis.**
  Andrew Lawrence. Stroke and Dementia Research Centre, St George's University of London. United Kingdom.
- **Identifying potential blood gene expression markers for Postpartum Psychosis.**
  Montserrat Fusté. King's College London - IOPPN. United Kingdom.
- **Insights into postpartum psychosis pathophysiology from a new mouse model.**
  William Davies. Behavioural Genetics Group – Cardiff University . United Kingdom.