PARALLEL SESSION 4 – FRIDAY 21ST 2019, 15h30 – 17h00

Mental health issues in diabetes mellitus and metabolic diseases: Update 2019

- S. Atasoy: Psychodiabetology of metabolic diseases: recent updates
- K.-H. Ladwig: Inverse Relationship between Social Isolation and Type 2 Diabetes Incidence in People with Obesity: Findings from the MONICA/KORA Prospective Cohort
- X. Cai: Loneliness and obesity in old women are associated with lower plasma oxytocin levels: The combined impact of mental and physical distress on the neuroendocrine system
- Ch. Sujana: Generalised anxiety disorder and incident type 2 diabetes in KORA F4/FF4 Study
- H. Johar: Chronic inflammation contributes to cortisol-induced hyperglycemia: Findings from the KORA Age study

Theme
- Psychobiology of stress-induced type 2 diabetes mellitus and metabolic disorders
- Synergistic effects of psychosocial risk factors with metabolic risk factors.

Takeaways
- Our approach is to use population-based data to investigate association within the general population.
- We explore in details of the behavioural and psychobiological pathway of diabetes and metabolic syndromes.
- For example, one of our investigation demonstrated the significance of considering inter-individual differences for psychosocial risk factors of type 2 diabetes mellitus: surprisingly, obese participants with a higher social network had an increased risk of type II diabetes in comparison to obese participants who were socially isolated.
- Dysregulation in neuroendocrine and inflammatory pathways have been linked to be associated with poorer psychosocial and metabolic health outcomes.

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Co-chair: Johannes Kruse, Director Department of Psychosomatic Medicine and Psychotherapy, University of Gießen and Marburg, Germany, DE
Psychodiabetology of metabolic diseases: recent updates

Aim
Metabolic disorders as significant risk factors for type 2 diabetes mellitus (T2DM) incidence have been established, but the psychobiology associated between synergistic psychosocial and metabolic risk factors are not thoroughly investigated.

Methods
Using up to 10,000 participants from the population-based MONICA KORA study to investigate potential pathways between psychosocial and metabolic risk factors on the risk of T2DM incidence, various statistical methods including Cox Proportional Hazards models and logistic regression analyses were conducted, with adjustment for potential confounders. Within the same study platform including over 1000 participants, the link between the risk factors and various biomarkers (i.e. Cortisol, Oxytocin, Interleukin-6, and HbA1c) were examined by using linear regression models and mediation analyses.

Results
Significant associations between psychosocial risk factors and the onset of T2DM were found and the presence of additional metabolic factors amplified the negative effect of psychosocial factors. In one investigation, a synergistic effect between loneliness and obesity might result in lowered plasma oxytocin levels. In two further investigations, inflammation played a significant mediating role in the relationship between psychological distress and metabolic dysregulation.

Conclusion
In summary, the current investigations provide evidence for the need to integrate a complex multitude of psychosocial and metabolic risk factors, as well as biomarkers which could have widespread implications for understanding the progression towards T2DM.

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Inverse Relationship between Social Isolation and Type 2 Diabetes Incidence in People with Obesity: Findings from the MONICA/KORA Prospective Cohort

Aim
Social isolation increases the incidence of type II diabetes (T2DM) but its’ effect on the association between obesity and T2DM remains unknown.

Methods
In a sample of 9,448 participants followed for a mean of 15.3 years (186,158.5 personyears) from the prospective MONICA/KORA population-based cohort conducted in Germany, we investigated the impact of social isolation, conceptualized by the Social Network Index (SNI), and obesity (Body Mass Index ≥ 30) on the incidence of T2DM using stratified Cox Proportional Hazards Regression adjusted for additional risk factors.

Results
In the general population, social isolation increased the risk of T2DM by 20% (HR 1.20, 95% CI 1.05 to 1.34; p=.005) whereas obese participants were at six times higher risk of T2DM than non-obese participants (HR 6.17, 95% CI 4.91-7.75, p<0001). Following indication of a multiplicative interaction between social network and BMI, an inverse association where socially-connected obese participants had higher T2DM incidence than socially-isolated obese participants in reference to their normal weight counterparts was found (HR: 5.20, 95% CI 3.88-6.96; p<.0001 vs. HR: 7.88, 95% CI 5.44-11.43; p<.0001). This finding was justified by an accumulation of psychosocial stressors and lower life satisfaction in socially-connected obese participants (26.8%) in comparison to socially-connected normal weight participants (33.0%) and overweight participants (28.0%, p=.005).

Conclusion
The present investigation disclosed that although social isolation generally increases the risk of T2DM, socially-connected obese participants pose a higher risk of T2DM than socially-isolated obese participants, potentially as a result of stigmatization towards obesity leading to negative social interactions.

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Loneliness and obesity in old women are associated with lower plasma oxytocin levels: the combined impact of mental and physical distress on the neuroendocrine system

Aim
Oxytocin has been recognized for its role in social relationship and energy regulation. Whether obesity could moderate endogenous oxytocin levels in response to subjective social interaction deficit (loneliness) is unknown. We aimed to investigate oxytocinergic stress response to loneliness in a representative older population considering the comorbidity of obesity.

Methods
We analyzed non-fasting plasma oxytocin in 954 participants (464 women, 490 men) aged from 63 to 95 years of the cross-sectional KORA-Age study. Loneliness was assessed using a short version of the UCLA-Loneliness-Scale in a personal interview. General linear models adjusted for age were conducted to investigate the impacts of loneliness and obesity and their interaction on oxytocin levels separately for women and men. Four multiple linear regressions stratified for sex, adjusted for potential demographic, physical and psychosocial confounders, further quantified the effects of loneliness and obesity on oxytocin levels.

Results
Oxytocin appeared to be unaffected by loneliness or obesity. Nevertheless, oxytocin was significantly decreased among lonely and obese women (mean, 95% confidence interval (CI): 179 (150 − 213) pg/ml) comparing to women who were neither lonely nor obese (mean, 95% CI: 228 (198 - 262) pg/ml). The decrease in oxytocin associated with obesity and loneliness persisted after adjusting for confounders (β = -0.28, standard error = 0.12, P = 0.019). This association was not observed among men.

Conclusion
The findings showed a cumulative effect of loneliness and obesity in lowering plasma oxytocin levels, and indicated an oxytocinergic pathway mediating loneliness and obesity to higher metabolic and cardiovascular susceptibility in women.

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Generalised anxiety disorder and incident type 2 diabetes in KORA F4/FF4 Study

Aim
We aimed to investigate if generalized anxiety disorder (GAD) presented as a risk factor for incident type 2 diabetes mellitus (T2DM) and to understand the effect of biological and behavioural factors on the association.

Methods
A longitudinal analysis examining the association between GAD and incident T2DM was conducted among 1688 participants (women:875, 51.8%; men:813, 48.2%) of two population-based KORA surveys conducted in 2006–2008 and followed up until 2013-2014 with a mean age of 51.2±10.6. GAD was assessed at baseline using the Generalised Anxiety Disorder-7 which dichotomised using a validated cut-off point of 10. Odds ratios (OR) were estimated using logistic regression models.

Results
Among 1688 study participants without any diabetic conditions at baseline, 113 (6.7%) suffered from GAD. From which, 14 (12.4%) participants developed T2DM at follow-up. GAD at baseline was significantly associated with incident T2DM in a model adjusted for age, sex and education (OR=2.40; 95%CI, 1.29-4.48; P=0.006). After fully control for lifestyle, metabolic conditions, C-reactive protein (CRP), antidepressants, depression and other psychosocial factors, the association remained significant (OR=2.31; 95%CI, 1.12-4.77, P=0.024). As higher CRP levels were observed among GAD vs no-GAD participants (P for difference=0.026), we further examined whether GAD is associated with T2DM through CRP. We did not find CRP as a significant mediator after controlling for lifestyle and metabolic factors.

Conclusion
Our findings suggested GAD as a risk factor for T2DM, independently of behavioural and metabolic factors. More research investigating inflammation using different biomarkers is needed to elucidate the biological mechanism underlying anxiety-diabetes association.

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Chronic inflammation contributes to cortisol-induced hyperglycemia: Findings from the KORA Age study

Aim
Although stress-induced increases in immune and endocrine responses have been implicated in glucose metabolism, the cross-talk between the two systems remains poorly understood. The study aimed to investigate the synergistic effect between cortisol and inflammation on hyperglycemia in a representative sample of community-dwelling older people.

Methods
The associations between cortisol (salivary and serum), Interleukin-6 (IL-6) and glycated hemoglobin (HbA1c) were analysed in a total sample of 394 men and 364 women (mean age=75 ± 6.3 years, 65 - 90 years). Using mediation analysis, we estimated the proportion explained by IL-6 on the relation between cortisol levels and HbA1c.

Results
Flatter diurnal cortisol slope (DCS) was significantly associated with a 21% increase in IL-6 concentrations in the hyperglycemic state group compared with control subjects (P =0.04). IL-6 significantly mediated the association between dysregulated cortisol levels (i.e. flatter DCS and higher late-night salivary cortisol) and elevated HbA1c. However, there was no significant indirect effect of Cortisol Awakening Response (CAR) through inflammation.

Conclusion
In our sample, the relation between flatter diurnal cortisol secretion patterns and hyperglycemia to a large extent was explained by IL-6 levels. The paradigm of subclinical inflammation-mediated cortisol response on glucose metabolism could have widespread implications for understanding type 2 diabetes mellitus.

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