Depression and Insulin Resistance: Additional Support for the Novel Heuristic Model in Perimenopausal Depression

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These data has not been presented before.

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Acknowledgements
We thank the late professor Paula Rantakallio (launch of NFBC1966), the participants in the 31yrs and 46yrs studies and the whole cohort 1966 team, which includes managers, nurses, clerical workers, research scientists and IT-personnel.

Grant sources:
NFBC1966 received financial support from University of Oulu Grant no. 65354 and no. 24000692, Oulu University Hospital Grant no. 2/97, 8/97, and no. 24301140, Ministry of Health and Social Affairs Grant no. 23/251/97, 160/97, 190/97, National Public Health Institute, Helsinki Grant no. 54121, Regional Institute of Occupational Health, Oulu, Finland Grant no. 50621, 54231, ERDF European Regional Development Fund Grant no. 539/2010 A31592), and NIH/NIMH (5R01MH63706:02). Eskola PJ has received a personal grant from Finnish Medical Foundation Duodecim.

Potential conflicts of interest:
MT was reimbursed by H. Lundbeck A/S, GSK, and Servier for attending conferences, was paid by H. Lundbeck A/S, GSK, and Servier for speaking on different educational occasions, has received advisory panel payments from H. Lundbeck A/S, Servier, and Pfizer for separate meetings, and has been a minor shareholder in Valkee Ltd. PJE has received a travel stipend from HIMSS. JJ, MRJ, SKK, RA, KP and JA report no competing interests.
Letter to the Editor

Gordon et al. recently proposed a novel heuristic model for the etiology of perimenopausal depression in the *Journal* (1). The model suggests that ovarian hormone fluctuation during menopause transition may cause hypothalamic-pituitary-adrenal (HPA) axis dysregulation, which increases interpersonal vulnerability and psychosocial stress sensitivity leading to added risk of depression.

Diabetes and its precursor, insulin resistance (IR) are associated with depression, but some previous results are conflicting regarding differences in the association by age and gender (2). Furthermore, it has been suggested that the comorbidity of depression and diabetes might be partly explained by shared etiopathogenesis via the HPA axis (3). On the other hand, it has been suggested that menopause related loss of ovarian function loss increases IR (4). Consequently, it is reasonable to hypothesize that association between depression and IR appears in women undergoing menopausal transition.

We examined depression symptoms and insulin resistance associations (DIRA) in a prospective study setting utilizing the Northern Finland Birth Cohort 1966 (NFBC1966, N=12 231, http://www.oulu.fi/nfbc). We compared the DIRA differences between genders at two time points, at 31 and 46 years, i.e. before and during the menopausal transition (5).

According to our present findings (Figure 1), DIRA is non-existent in women during reproductive age, but emerges during the menopausal transition and is seen statistically significantly in the severe depressive symptoms. DIRA is seen at both ages in men, but the association is seen also with moderate symptoms at the age of 46 years.
Our results support the novel model (1) by linking in IR. To our knowledge, this is the first report demonstrating the effect of menopause on DIRA. We postulate that the present DIRA shift in women stems via the HPA axis (3, 4) triggered by hormonal fluctuations in menopause transition (1). The non-existent DIRA among women at 31 years may be explained by the protective effect of estradiol on the HPA axis. While fascinating, these findings still leave us observing the phenomenon at a distance, since our data does not allow direct pathway scrutiny.
References


The insulin resistance was defined using homeostasis model for insulin resistance (HOMA2-IR), and depressive symptoms were quantified by Hopkins Symptom Checklist-25 (HSCL-25); depression subscale. Multinomial logistic regression model was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI). Subjects in the highest decile of IR were compared with the rest. The model was adjusted for education (basic, secondary and tertiary), smoking (never, ex-smoker and current smoker), alcohol consumption (grams per day), physical activity (frequency of brisk physical activity). The authors were given access to the NFBC 1966 database, and these results are based on the data collected at 31 and 46 years (n=5653 and n=5021, respectively).