Gene-environment Interaction Between Estrogen Receptor (ER) SS, ApoE and Air Pollution On Cognitive Performance in an Elderly, Female Cohort.

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Introduction: In the brain, estrogen plays an important role in neural plasticity and its decline during menopause might result in cognitive impairment and predispose to the development of dementia. Two estrogen receptors – α and ß – mediate estrogen actions either as ligand-activated dimeric transcription factors or as membrane-embedded ER monomers.

Objective: To analyze ERß-variants and ApoE-genotype in the population-based SALIA cohort of 834 non-demented, elderly women.

Aims: We aimed to explore, whether ERß variants may impact on cognitive performance in interaction with air pollution and APOE.

Methods: DNA was isolated from lymphocytes. ApoE-epsilon-variants and ERß SNPs rs944045, rs1256062, rs10144225 and rs2274705 were determined by LCG /KBioscience (Hoddesdon, UK). All participants were assessed for cognitive impairment by the CERAD-Plus test battery. Subtests were merged to a total z-score, that corrected for gender, age and time of education. Long-term exposure to air pollution was backextrapolated from data collected by monitoring stations using a geographic information system.

Results: SNP analysis revealed that 3 ERß variants (rs1256062, rs10144225 and rs2274705) were significantly correlated with lower CERAD z total scores and especially with decline in episodic memory. These effects were strengthened in APOE-epsilon-E4 carriers. Air pollution (NO_2, PM2,5) did not worsen the CERAD z total score of the women, but interacting with the ERß variants PM2,5 affected their visuoconstructive practice and NO_2 their semantic memory .

Conclusion: In this population-based, prospective study a gene-gene interaction effect of ApoE and ERß on cognitive performance appeared. Moreover, significant gene-environment interactions on cognition were found for air pollution.