

Paper presented at the International Association of Gerontology and Geriatrics European Region Congress, Gothenburg, Sweden, May 2019.

Gene-Environment Interplay to Explain Health Heterogeneity: Results from the Swedish Twin Registry

Nancy Pedersen [Stockholm, Sweden]¹, Anna Dahl Aslan [Sweden]²

Karolinska Institutet¹, Jönköping University²

There are a number of ways in which one can test for gene-environment interplay in health heterogeneity. If one has genotypes available for a reasonably large sample, as is the case in several of the NEAR cohorts, the direct test of an interplay is to test for the interaction between a genotype, an exposure of interest, and a health outcome. In this way, one could determine whether the importance of, e.g. SES on cognitive health depends on whether or not one is genetically susceptible (carrier of the *APOE* ϵ 4 allele). However, one does not always have an a priori hypothesis about whether the effect of genes differs as a function of an exposure, or even know which exposures may interact with the genes. Twin studies provide a valuable means of evaluating the presence of gene-environment interplay in the absence of having measured genotypes or even specific exposures at hand. By applying Fisher's 1925 test among identical twins (the difference between mean squared pair differences for a trait and the mean absolute pair differences squared), one can obtain evidence for G-E interplay. In this fashion, studies of Swedish twins have demonstrated G-E interplay for depressive symptoms, BMI, grip strength and some cognitive tests, and that the interplay varies as a function of age. Classical twin modeling using information from both identical and fraternal twins indicates that childhood SES moderates genetic influences on adult level of verbal cognitive abilities, but not on cognitive change or other cognitive measures. Furthermore, *APOE* may be a "variability gene", contributing to health heterogeneity. Other developments, including the use of polygenic risk scores in the quest for understanding G-E interplay, and potential applications within NEAR will also be presented.