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GxE contributions to cognitive aging: An MZ twin pair comparison

Chandra Reynolds, University of California Riverside; Nancy Pedersen, Karolinska Institutet

How interactions between genes and environment affect human aging processes are not well understood. However, their potential importance can be gleaned from both animal and human studies where GxE interactions may change with age. Longitudinal studies of twins may be informative to consider GxE for normative cognitive aging by comparing within MZ pair differences in trajectories by genotype to identify responsivity of particular genotypes to environments. We evaluated multiple cognitive domains (verbal, spatial, speed as well as memory) and multiple genes in lipid and inflammatory pathways that may be of potential importance to normative cognitive performance and decline. In illustrative analyses we fitted piecewise growth curves to data from three longitudinal Swedish studies of aging (SATSA, OCTO-Twin, and Gender), with data collected up to six waves across 19 years. Estimates of growth curve features were retained and evaluated in subsequent comparisons of MZ twin pairs. Transformations to reduce non-normality were applied and inverse standard errors served as analysis weights. Heterogeneity tests for verbal, spatial, memory and perceptual speed tests among MZ pairs indicated mixtures of distributions for cognitive change before and after age 75 for Synonyms, Block Design, and Thurstone Picture Memory, and after age 75 for Symbol Digit. These results served as a first indication of possible GxE interaction, suggesting that responsiveness to environments, perhaps indicative of plasticity, is evident for cognitive change. Intrapair differences were then evaluated for association. MZ pairs with the APOE e3e3 genotype were more variable in decline

rates before age 75 than those who carried the e2 or e4 alleles (e.g., Block Design). Apart from APOE, SORL1 risk scores may predict differential variability in verbal and spatial trajectories. Lastly other lipid pathway genes may be important to variability in cognitive change after age 75 (e.g., APOB, LRP1, LDLR). Supported by AG037985 and AG028555.