MZ within pair tests of gene-environment interaction: examinations of health, well-being and cognitive performance

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Gene-environment interplay (GxE) may contribute across multiple domains, including cognition, health, and well-being traits. We evaluated GxE interactions for depressive symptoms, BMI, and cognitive performance (verbal, spatial, memory, and perceptual speed) available in eight twin studies in the IGEMS consortium from Denmark, Sweden, and the US (ages 25–102). We highlight the use of GxE models that evaluate mixture distributions of within pair differences in identical (MZ) twin pairs [see Fisher, R. A. (1925). The Resemblance between Twins, a Statistical Examination of Lauterbach's Measurements. Genetics, 10, 569–579; Martin, N. G., Rowell, D. M., & Whitfield, J. B. (1983). Do the MN and Jk systems influence environmental variability in serum lipid levels? Clinical Genetics, 24, 1–14]. Trait scores were first adjusted for sex, age and country, and rank-normalized. Pooled analysis of within pair heterogeneity suggested possible GxE for the full sample, within country, and within sex for depressive symptoms (p = 1.07E-03 to 4.27E-25) and for BMI (p = 2.26E-06 to 5.43E-19). The cognitive traits demonstrated significant evidence for GxE in the full sample (p = 3.95E-03 to 1.42E-12), and similar patterns were observed across country and gender. Tests conducted within age bands (\50, 50–59, 60–69,70–79, 80+) suggested significant GxE for depressive symptoms (p = 1.26E- 04 to 1.66E-09) until age 80 (p = 2.48E-01), that peaked during ages 60–69 years (effect size r = 0.26). For BMI, patterns of within pair heterogeneity were nonlinear over age with peaks before 50 and after 70 years (effect size r's = 0.19–0.22). With respect to cognition, trends suggested GxE peaks in midlife (\60 years) for speed but in later adulthood for verbal traits ([60 years). Age periods when GE interplay peaks for health, wellbeing and cognitive traits may signal salient phases when age-related change is observed.