Investigating time-varying genetic influences on body length trajectories from infancy to adolescence

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Abstract

Body length from birth to late adolescence is shaped by genetic influences that vary across development. Using 85,080 repeated body length measures from 7,181 genotyped participants in the Avon Longitudinal Study of Parents and Children (ALSPAC), we applied a random regression model with linear splines to estimate a genetic covariance matrix across birth to 18 years. SNP-based heritability (h^2_{SNP}) was lowest at birth, 17% (SE = 3%), and peaked around 14 years (41.6% [SE = 4.6%]). In addition, the estimated h^2_{SNP} of the linear rate of change (slope) from birth to 14 years and from 14 to 18 years was 41.7% (SE = 5.0%) and 26.5% (SE = 5.6%), respectively. The genetic correlations (r_g) between early and later ages were moderate to strong (e.g. the lowest r_g across all ages is 0.68 [SE = 0.1] between birth and age 14). Eigen decomposition of the genetic covariance matrix revealed two major patterns: one representing stable genetic influences across ages (explaining 67.9% of the variance) and another reflecting a reversal in the magnitude of genetic effects before and after age 14 (31.4%). A reduced genetic relationship matrix based on only ~12,000 adult height-associated loci captured most of the genome-wide genetic variance across the trajectory. Replication in the Born in Bradford (BiB) cohort confirmed similar heritability estimates in both European and South Asian ancestry groups from birth to year 10. Our findings demonstrate dynamic age-dependent genetic influences on body length and highlight the continued relevance of adult height-associated loci throughout early growth.