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Phenotypic and genetic study of a wellbeing factor score in the UK Biobank and the impact of childhood maltreatment

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ABSTRACT:

Wellbeing is an important aspect of mental health, distinct from the absence of mental illness. Wellbeing is moderately heritable, and large-scale genome-wide association studies (GWAS) have identified specific wellbeing-related variants. While there are various subcomponents of wellbeing, measured with different instruments and assessing different facets of the same spectrum, they are usually correlated. Therefore, a score derived from multiple questions has potential to capture a more stable and heritable wellbeing phenotype, thereby increasing power for genetic and phenotypic studies. We employed the population-based UK Biobank baseline dataset of self-report questionnaires to create a wellbeing factor score derived from indices of: happiness and satisfaction with family, friendship, financial and health; using principal component analysis. A GWAS was performed in 129,237 Caucasian participants using the derived wellbeing score, followed by polygenic profiling in an independent sample (n=23,703) to predict the wellbeing score and correlated phenotypes. The wellbeing score, its subcomponents and some negative indicators of mental health (including neuroticism, depressive symptoms, and loneliness) were compared in terms of phenotypic and genetic correlations. Lastly, the impact of childhood maltreatment on the wellbeing score was investigated. We identified four genome-wide significant GWAS hits for wellbeing. SNP heritability was ~8.6%, higher than each subcomponent. The wellbeing score had the highest phenotypic and genetic correlation with mental health phenotypes compared to individual wellbeing items, except for neuroticism on happiness. Additionally, childhood trauma significantly reduced wellbeing scores, with a moderate negative genetic correlation (~-0.56). Thus, a wellbeing index can elucidate phenotypic and genetic relationships with mental health and is moderated by trauma.

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