

Commentary: The strength of multivariate twin studies: testing for shared and distinctive aetiology among different sets of behavioural traits – reflections on Lewis et al. (2014)

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The accompanying article by Lewis, Haworth and Plomin (2014) on the relationship between variation in normal personality and adolescent behavioural problems is important in at least two aspects: it offers an understanding of the causes of such associations, and through its design demonstrates how twin studies can go beyond estimating the contribution of the genome to variation in complex human traits to offer new insights into the aetiology of covariation among multiple traits.

Multiple traits are often referred to as phenotypes in genetic studies: an observed set of traits or characteristics. In contrast, unobserved traits are referred to as latent factor scores: these can be genetic or environmental, for example. Thus, a Phenotype score = Genetic score + Environmental score, and under a simple model assuming no complex genotype-by-environment interplay: the variation (Phenotype) = variation (Genome) + variation (Environment).

The article by Lewis et al. describes how the core dimensions of personality (based on the five factor model of personality) together account for all genetic variation in several key aspects of adolescent behavioural problems. Even though the observed correlations between personality and behavioural problems are modest, the multivariate genetic analyses strongly suggest that the genetic correlations (referring both to the correlations between additive genetic factors and nonadditive genetic factors), one should keep in mind that to obtain the phenotypic correlations, the genetic correlations (e.g. between anxiety and neuroticism) are multiplied by the square root of the heritability of these traits. Turning to the heritability estimates in table 4 of Lewis et al. (2014), we note that these are low (especially for personality, where these tend to be lower than what often is reported) and that the confidence intervals around the estimates often include zero. This implies that the point estimates of the genetic correlations are probably rather imprecise as well. The important message, however, is that through the twin design there is an insight that much, or even all, genetic

variation in the problem behaviours included in the assessment is shared with personality.

This also poses an interesting question: is there nothing left to explain for other dimensions of personality such as the Sensation Seeking Scales (e.g. behavioural disinhibition, boredom susceptibility) as proposed by Zuckerman? These personality scales are nearly orthogonal to the five personality scales included in Lewis et al. (2014) and it would seem remarkable that they do not contribute to adolescents' problems. Although the scales that are used in the Lewis et al. have relatively few items, which may explain their low heritability as the heritability of a phenotype cannot exceed its reliability, a strength of the study is that the measures of personality and problem behaviour were collected approximately 6 months apart, thereby avoiding correlations that arise through response tendency.

The multivariate methodology as presented in Lewis et al. (2014) takes as input the resemblance within twin pairs across traits: how well does personality in one twin predict behavioural problems in the co-twin? If the association between two phenotypes is caused by genetic correlations, the degree of prediction will be higher in monozygotic than in dizygotic twin pairs. This very general approach can be generalized to other areas of child psychology and psychiatry. Franić et al. (2013), for example, discussed the role that quantitative genetic methodology may play in assessing and understanding the dimensionality of psychological instruments, such as in the often-used Child Behavior Check List (CBCL) by studying the relationship between the observed covariance structure among items on the one hand, and the underlying genetic and environmental factor models giving rise to such structures on the other. This relationship may be such that it hampers obtaining a clear picture of phenotypic dimensionality. When, for example, genetic and environmental influences underlying the observed covariance structure differ from each other in structure and dimensionality, establishing phenotypic dimensionality can be problematic, and may only be resolved by using quantitative genetic modelling

to uncover the (possibly different) dimensionalities of the underlying genetic and environmental structures.

The multivariate modelling approach as presented in Lewis et al. (2014) leads to new insights into the genetic and environmental correlation structure, but is only the first, most general type of decomposition of a correlation matrix between multiple traits. Nested under this general, descriptive, model are multiple submodels which, if they fit the data, offer additional explanations as to why traits cluster together. For example, if personality has a causal influence on problem behaviour, and if personality is heritable, then it should follow that problem behaviour is also heritable and that the heritability is a function of the strength of the causal relationship. Employing this framework, De Moor, Boomsma, Stubbe, Willemsen and de Geus (2008) showed that the often-reported association between lack of exercise and depression is unlikely to reflect causality and is more likely to reflect genetic pleiotropy.

Thus, multivariate twin modelling opens new avenues for testing causality in observational data. For example, evidence has accumulated that low birth weight is associated with unfavourable outcomes later in life, including metabolic diseases. It has been debated whether such associations are due to a programmed response to intrauterine malnutrition or due to genetic factors influencing both birth weight and metabolic disorder. Twin studies suggested that these associations are, at least in part, due to genetic factors, because of the significant genetic correlations between birth weight and later outcome measures. Such findings can now be followed up with measured genetic variants. One of the first meta-analyses of six genome-wide association (GWA) studies obtained a signal in the ADCY5 gene for birth weight (Freathy et al., 2010). Correlated SNPs in ADCY5 were also implicated in the

regulation of glucose levels and susceptibility to type 2 diabetes, providing evidence that the association between lower birth weight and type 2 diabetes later in life has a genetic component, distinct from the role of programming by, for example, maternal nutrition.

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