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LETTER TO THE EDITOR

Life events moderate variation in cognitive ability (*g*) in adults

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The heritability of general cognitive ability (*g*) in adults is estimated to lie approximately between 75 and 85%.[1] Despite this overwhelming indirect evidence of 'genes for *g*', only a handful of genes have been identified so far, together explaining $< \sim 5\%$ of the genetic variation.[2] Several reasons have been suggested for this 'missing heritability',[3] including the presence of gene–environment interactions (GEI). We have investigated the presence of GEI for measured Life Events and *g*, in a population-based sample of adult twins and their siblings ($N = 560$).

The reported large heritability estimates for *g* are derived from classical twin studies, in which additivity of genetic and environmental effects is assumed; implying heritability estimates are equal across environmental conditions. Non-additivity of genetic and environmental effects (that is, GEI), conversely, implies that genes control an individual's sensitivity to environmental influences, or environmental factors moderate gene expression. If GEI is present, the extent to which genes and environment cause variation in *g* varies across environmental conditions, and a single heritability estimate is no longer accurate.[4] Consequently, assuming the absence of GEI may lead to biased estimates of the relative importance of genetic and environmental influences.[4] Moreover, when genetic effects vary across environmental conditions, an environmentally stratified design might seriously improve gene-finding success when researchers focus on those environmental conditions wherein the genetic effects are largest. Gene-finding attempts for *g* would thus benefit from studies that elucidate the environmental circumstances for which genetic effects are largest.

Few studies have provided evidence for GEI in the context of *g* in children and adolescents, thus demonstrating increased heritability in children from highly educated parents and in children with high socio-economic background. To date, studies on GEI in adults, where heritability estimates of *g* are largest,[5] are rare, with two studies hitherto showing evidence of modest moderation on environmental influences but not on genetic influences.[6,7]

We first determined whether there is a correlation between intrapair sum and intrapair difference scores for *g* in 136 complete adult monozygotic twin pairs, as such a correlation would imply non-additivity of latent genetic and environmental factors.[8] This correlation was 0.20 ($P = 0.02$), suggesting that adults of higher cognitive ability are more sensitive to the environment. We then focused on moderation effects of *measured* environmental effects, that is, 19 measures of positive, negative, and neutral Life Events on genetic and environmental influences of *g* within a population-based sample of 560 twins and their non-twin siblings[9] (age 23–75 years). Statistical analyses were conducted in which linear and non-linear moderation by the 19 Life Events on genetic and environmental influences was tested. Results demonstrated modest negative moderation of genetic factors by several Life Events (i.e., genetic influences were smaller for subjects who experienced *Birth of a child, Breaking up with friends/relatives, Death of friends/relatives* and *Retirement*), and considerable moderation of these Life Events on the overall environmental influence (*Birth of a child, Breaking up with friends/relatives, Severe trouble with friends/relatives, Death of friends/relatives, Severe offence, Being fired, Unemployment* and *Retirement*), with direction depending on the specific Life Event. Estimates of genetic and environmental influences, as a function of the exposure to a particular Life Event, are depicted in Figure 1. Exposure to *Severe illness*, *Divorce*, *Receiving mental health treatment*, *Robbery*, *Sexual abuse*, *Marriage*, *Drivers license*, *Graduation*, *Promotion* and *Changing schools in childhood* did not moderate the variance components of *g*.

Although these results need replication, the broad heritability of *g* ranged from only 9% to above 90% across levels of positive, negative, and neutral Life Events, suggesting that the extent to which genetic and environmental influences affect individual differences in *g* in adults is not equal across the entire population, but varies with exposure to Life Events.

This conclusion is important in the context of gene finding studies for *g* as linkage and association studies generally assume additivity of genetic and environmental factors, implying that genetic effects are equal under various environmental circumstances. We show that this assumption does not always hold. Ignoring the complex interplay between genes and environment in gene-finding studies may partly explain the lack of success in the identification of genes for *g*. Gene finding studies should thus include GEI effects to increase their chances of success.

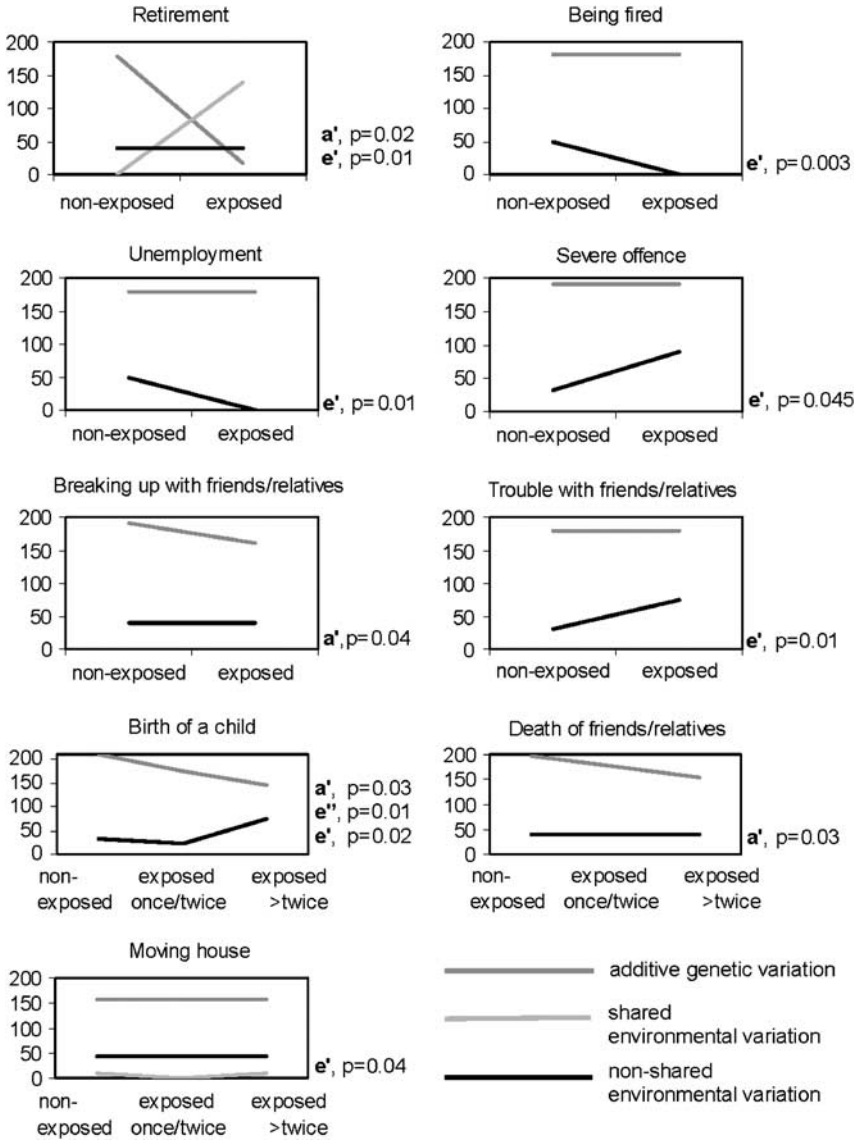

Figure 1 Unstandardized variance components of *g* as a function of the exposure to different Life Events. The figures are based on the most reduced models, that is, on models in which all non-significant effects were eliminated from the model. Unstandardized variance components refer to the *absolute* contribution of additive genetic effects, shared environmental effects and non-shared environmental effects to variation in *g*. *Additive genetic variation* represents additive effects of alleles summed over all genetic loci. *Shared environmental variation* represents environmental influences that render members of the same family more alike. *Non-shared environmental variation* represents all environmental influences that result in differences between members of a family, including measurement error. *P*-values correspond to significance levels of *non-linear* moderation of additive genetic effects (***a''***), shared- (***c''***) and non-shared environmental effects (***e''***) and significance levels of *linear* moderation of additive genetic effects (***a'***), shared- (***c'***) and non-shared environmental effects (***e'***). Please note that the heritability (h^2) is defined as the ratio of the genetic variance to the total variance. We refer to the Supplementary information on the Molecular Psychiatry website for figures of standardized variance components, that is, the relative contribution of additive genetic effects (h^2), shared environmental effects and non-shared environmental effects to variation in *g*.

Conflict of interest

The authors declare no conflict of interest.

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References

1 Plomin R. *Nature* 1999; **402**: C25–C29.
2 Posthuma D, de Geus EJC. *Curr Dir Psychol Sci* 2006; **15**: 151–155.
3 Maher B. *Nature* 2008; **456**: 18–21.
4 Purcell S. *Twin Res* 2002; **5**: 554–571.
5 Haworth CM, Wright MJ, Luciano M, Martin NG, de Geus EJ, van Beijsterveldt CE *et al. Mol Psychiatry*, advance online publication 2 June 2009; doi: 10.1038/mp.2009.55.
6 Kremen WS, Jacobson KC, Xian H, Eisen SA, Waterman B, Toomey R *et al. Behav Genet* 2005; **35**: 417–433.
7 van der Sluis S, Willemsen G, de Geus EJ, Boomsma DI, Posthuma D. *Behav Genet* 2008; **38**: 348–360.
8 Jinks JL, Fulker DW. *Psychol Bull* 1970; **73**: 311–349.
9 Vinkhuyzen AA, van der Sluis S, de Geus EJ, Boomsma DI, Posthuma D. Genetic influences on 'environmental' factors. *Genes Brain and Behavior*; advance online publication 24 November 2009; doi: 10.1111/j.1601-183X.2009.00554.x.

Supplementary Information accompanies the paper on the Molecular Psychiatry website (http://www.nature.com/mp)