Gene–Environment Interplay in Adulthood

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Introduction

The topic of gene–environment interplay has long been of interest to behavioral geneticists (Waddington 1942). In the 1970s, much of the critique of BG studies rested on the assumption in many biometrical models that there was no $G \times E$ interaction or GE correlation. The ability to test GE interplay has varied largely based on whether or not the models are solely based on anonymous variance components, or whether one has a measured G or a measured E. Indeed, adoption models were long thought to be the only way to get at GE correlation in absence of measured G or E. With the advent of the moderation model by Purcell (2002) and improvements (Van der Sluis et al. 2008), a wave of interest in using moderator models began, where variance components could be tested as a function of a particular “environment.” Even more attention was brought to the field when Caspi et al. published their findings in *Science* (2003), with a specific candidate gene and a variety of measures of E, i.e. stressful life events, on multiple indicators of depression and depressive symptoms.

The Behavior Genetics Association has seen an increase in presentations addressing various forms of GE interplay, not the least at the association’s annual meetings. For example, in 1995 there were only two papers at the annual meeting that addressed GE interplay, and at that time most of the work was conducted using mouse models of behavior. The number of papers focusing on various forms of GE interplay in humans slowly increased over the

following years (5 in 2000, 8 in 2005). The 2010 conference marks one of the first instances of the phrase “gene–environment interplay” appearing in the program (Arvey et al. 2010). By the 2015 conference, there were 18 papers and posters addressing GE interplay, using a variety of methodologies and applied to several phenotypes across the lifespan. We felt that the burgeoning production of papers related to GE interplay in humans, extending the methods and issues into adulthood, was worthy of a special issue of *Behavior Genetics*.

Contents of the special issue

Perhaps the most notable feature of the 12 articles in this issue is the variety of methodologies applied to address issues of GE interplay. These include everything from Fisher’s test of mixture distributions in MZ pairs from 1925, to moderation models as in Purcell (2002), item-level data methodology, evaluation of candidate genes, variations including an instrumental variables framework and genetic risk scores, gene-region based analyses with environment set association tests, reciprocal effects models (promoting accumulation of GE correlation), and finally, tests of phenotypic assortment and social homogamy.

There are also a variety of phenotypes evaluated in this issue, from cognitive abilities to depressive symptoms to self-rated health, objective measures of health (BMI and grip strength), trajectories of change, health-related behaviors (smoking), personality and pair-bonding. Some of these phenotypes are indeed considered as indicators of the environment (smoking, marital status), whereas other important moderators include neighborhood, ethnicity, and historical period.

The first two articles in this special issue use Fisher’s 1925 test based on MZ within pair differences to evaluate

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potential gene–environment interactions for cognitive performance, depressive symptoms, and BMI (*Reynolds et al.*), and for longitudinal trajectories of grip strength (*Petersen et al.*). Both articles follow-up evidence of $G \times E$ interaction with tests of whether *APOE* is a “variability gene” for these measures and represents the “G” in $G \times E$ effects.

Domingue et al. and *Schmitz and Conley* both address issues concerning smoking behaviors and the potential importance of historical context on genetic influences for smoking using data from the Health and Retirement Study, but in very different ways. Using a modified DeFries–Fulker approach with a GCTA based estimate of genetic similarity and a polygenic risk score (PRS) for smoking, Domingue tested hypotheses about differences in heritability of smoking as a function of birth cohort. Schmitz and Conley, on the other hand, tested whether men with a high genetic susceptibility to smoking (based on a PRS) are more likely to smoke than veterans inducted through the Vietnam-era draft lotteries, and whether post-service schooling modifies this interaction, using an instrumental variables framework.

Several of the articles focused on depression and depressive symptoms. *Molenaar et al.* investigated whether non-linear effects of gene by environment interaction mask the common environmental variance for depressive symptoms in adulthood, using an item-level data methodology. Furthermore, they tested whether the interaction effects differed by gender, and found evidence for gene by common environment interaction in men.

Using a within person repeated measures design, *Arpa-wong et al.* revisited the 5-HTTLPR by stressful life events association with depressive symptoms. They found a main effect of recent stress, but the genotype by stress interaction was found only for some statistical models. Despite the power gained by using a repeated measures design, this study demonstrates the need for substantial sample sizes to find $G \times E$ interaction, particularly when multiple ethnicities are included. *Ware et al.* used yet another technique to identify potential gene by environment interactions for depressive symptoms, i.e. through evaluating gene regions previously identified, and applying those to both individual level and neighborhood level indicators of the environment. The results indicate the promise of these techniques, particularly in a multi-ethnic setting.

Unlike other papers in this issue that evaluated gene by environment interaction, *Beam et al.* used a reciprocal effects model to test whether a phenotypic exchange with non-shared environments ($P \leftrightarrow E$) leads to an accumulation of gene–environment correlation (rGE) and hence stability of late life depressive symptoms. There was no evidence of an underlying rGE, although widowhood explained stable within pair differences in depressive symptoms.

The last three articles in this issue also include marital status or relationships as a moderator (of self-rated health or personality) or as the result of phenotypic assortment. *Finkel et al.* found substantial gender differences in marital status as a modifier of variance in three subjective health measures. Whereas there was significant albeit modest marital status moderation of C and E components of self-rated health for women, marital status was a significant modifier of variance in all three subjective health measures for men. Marriage appears to be a buffering factor for variation in subjective health in men.

Using the Dyadic Adjustment Scale, *South et al.* tested whether relationship satisfaction moderated genetic and environmental variance for adult personality. Differing across the traits of the MPQ, moderation by relationship satisfaction was consistent with the diathesis stress model for well-being, social potency, and alienation, and suggested evidence for the bioecological model for aggression, constraint and traditionalism. No support was found for the differential susceptibility model.

Phenotypic assortment may be indicative of active rGE. *Horwitz et al.*, explored the extent to which phenotypic assortment and/or social homogamy can contribute to mate similarity, and found that phenotypic assortment, not social homogamy or convergence accounted for couple similarity in pair-bonding behavior. This demonstrates another form of GE interplay, in that individuals’ genetically based characteristics are involved in selection of mates with similar pair-bonding behavior.

Conclusions

Fifteen years ago, in a review of environmental influences on cognition in adulthood, we lamented the fact that although methods for evaluating GE interplay were being developed, their implementation was limited (*Finkel and Pedersen 2001*). This issue of the journal is a testament to the continuing advancement and vitality in the field of behavior genetics, as researchers grapple with increasingly sophisticated models of complex human behavior. We look forward to seeing what the next 15 years will bring.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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