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Confounding, Causal Inference, and the Nature of Parent Effects: The Utility of the Adoption Study Design

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Parents have long been seen as playing a fundamental and implicitly causal role in shaping the children they rear. A focus on parenting is evident in the premier journals in developmental science, which rarely publish an issue that does not include at least one article investigating the role of parents in child and adolescent socialization. Recent issues of *Developmental Psychology* and *Child Development*, for example, have featured papers reporting associations between parental monitoring and reduced adolescent drinking (Sasser et al., 2023), secure parent-child attachment and offspring prosocial behavior (Deneault et al., 2023), parental hostility and adolescent aggression (Yang et al., 2023), parental support and adolescent depression symptoms (McCurdy & Russell, 2023), and parents' history of healthy socioemotional development and their children's positive psychological development (Letcher, 2023). Indeed, one of the co-authors of this commentary has spent his whole career principally studying associations between the observed quality of parent-child interactions during early childhood and offspring outcomes, including examining how those associations are structured over increasingly long temporal intervals, into the years of adulthood (e.g., Fraley et al., 2013; Raby et al., 2015).

Developmental researchers are certainly aware of the admonition "*correlation does not imply causation*" and thus should be appropriately cautious in drawing causal inferences from research associating parenting with child outcomes, like the reports listed above. Nonetheless, as Rutter (2007) has argued, researchers are rarely satisfied with simply describing associations, but rather, seek approaches that allow them appropriately and robustly to infer the causal basis of psychological development. Yet the challenges in drawing causal inferences from observational developmental data are not easily addressed (Foster, 2010). The typical approach to confounding in observational studies, for example, is statistical, involving post hoc effect adjustment for a necessarily incomplete set of imperfectly measured (potential) confounders, covariates that may well be part of the (causal) developmental process the researcher is attempting to understand. As such, the problem of residual confounding cannot be readily eliminated with either statistical approaches like covariate adjustment (Sorjonen et al., 2021) or

design approaches like the analysis of within-person longitudinal change (Rohrer & Murayama, 2023), even though both can contribute to articulating causal hypotheses about the nature of observed associations.

The monograph by Reiss and colleagues (2023) describes the rationale and design of, and illustrative findings from, the Early Growth and Development Study (EGDS). EGDS addresses a major source of confounding in family socialization research by using an innovative behavior genetic design, an adoption study. There is a large and consistent behavior genetic literature showing that both parental behaviors and offspring outcomes are heritable, raising the possibility that associations between the two are partly attributable to genetic confounding (Plomin & Bergeman, 1991). In behavior genetics, this has been termed passive gene-environment correlation. If the adopted children had not been selectively placed in their rearing homes based on their birth background, the genetically mediated pathway that contributes to parent-offspring resemblance in intact families will have been eliminated in adoptive families. Reiss and colleagues summarize the evidence for the absence of selective placement effects in EGDS, providing confidence that the adoptive parent-offspring associations they observe are in fact environmentally mediated.

The scope and breadth of EGDS is nearly unprecedented in adoption research. The study began with the assessment of 561 adopted infants and nearly all their birth mothers, adoptive mothers, and adoptive fathers. Even a sizable minority of the birth fathers were recruited and assessed. Longitudinal assessment of the adopted individuals began when they were infants and now extends through their pre-adolescence and is likely to continue through their adolescence and early adulthood. Each assessment is extensive, covering the adopted individuals' mental and physical health, psychological and social functioning, and, importantly, their familial and extrafamilial environments. EGDS has already made numerous contributions to our understanding of family socialization processes, characterizing, for example, the effects of harsh parenting on effortful control, parental hostility on childhood aggression, and maternal symptoms of depression on offspring symptoms of internalizing psychopathology. We note in this context that the EGDS—focusing intensively on the early life course—complements our own work with the Sibling Interaction and Behavior Study (SIBS) cohort (McGue et al., 2007), which consists of 409 adoptive and 208 non-adoptive families examined prospectively from when the children were in late adolescence, with our most recent assessment occurring currently when the now adult children are approaching midlife.

Despite the value of the adoption design, it is important to recognize that an adoption study, like any other "natural experiment," can provide only a partial solution to the problem of confounding (Rutter, 2007). For example, EGDS researchers have sought to identify the impact of prenatal (e.g., *in utero* drug exposure) as well as postnatal exposures on child development. If adopted children were not selectively placed in their rearing homes, prenatal exposures can be assumed to be independent of the postnatal environment, addressing one major source of confounding in earlier research attempts to identify prenatal drug effects (e.g., Lester et al., 1997). Nonetheless, prenatal exposures cannot be expected to be independent of maternal genotype (Leppert et al., 2019), reintroducing the possibility of genetic confounding. EGDS researchers are aware of this issue and so adjust for covariates in their analyses of potential

prenatal effects. Access to birth father information, although incomplete, does raise the possibility of using what epidemiologists term a negative control. That is, observing birth-father characteristics, that likely had minimal impact on the prenatal environment, to be similarly correlated with offspring function as comparable birth-mother characteristics, which determine prenatal exposures, would be evidence against prenatal effects. Regardless, residual confounding likely remains so that causal inference cannot be certain.

Confounding is even an issue when investigating the relatively straightforward associations between adoptive parent behavior and offspring function. Take as an example the EGDS finding that hostile parenting is associated with offspring aggression. Because this association exists in adoptive families, in the absence of an association between birth parent antisocial behavior and adoptive parent hostility, it must be environmentally mediated, a critical observation for understanding the relevance of hostile parenting to child development. Nonetheless, the existence of this association in adoptive families does not, on its own, establish that hostile parenting is a cause of offspring aggression. Parental hostility is embedded within a broad matrix of risk, any node of which could be one of the potentially numerous causal drivers of the observed association. Perhaps the association is a consequence of the relationship of parental hostility with social class, parental psychopathology, marital dysfunction, or some other unknown factor.

Additional features of their design have provided EGDS researchers with unique ways for evaluating alternative explanations for the adoptive parent-offspring associations they observe. This is most notable when considering the possibility of reverse causation. Ever since the classic work of Bell (1968), developmental researchers have recognized that associations between parenting behavior and offspring function may reflect child rather than parent-driven effects. In EGDS, a child effect would be evident if adoptive parent behavior is correlated with birth parent characteristics since the latter constitute indicators of preplacement inherited risk that cannot have been influenced by adoptive parent behavior. In the case of adoptive parent hostility, a correlation with birth parent antisocial behavior was not observed, making it unlikely that adoptive parent hostility is a reaction to child aggression. Nonetheless, even if child aggression is not driving the association, other EGDS research using this method has implicated genetically influenced child impulsivity and social disengagement (as inferred from birth background) as factors that could trigger rearing parent hostility.

EGDS helps dispel the widespread misunderstanding that behavior genetic research is focused exclusively (or even is most informative) with respect to establishing the existence of genetic influences. Beginning with the landmark adoption research of Barbara Burks (1927), behavior geneticists have long been interested in environmental influence and especially the complex interplay of genetic and environmental factors in psychological development. The advantage of behavior genetic designs is that they can account for what is known to be a major potential source of confounding in family research, the shared genotype. In addition to EGDS, several innovative behavior genetic research designs that focus on environmental influence have been introduced and launched in the past decade, including studies of donor IVF babies (Rice et al., 2013) and the investigation of “genetic nurture” effects using molecular genetic data (Kong et al., 2018). Moreover, an innovative extension of EGDS involves the comparison of genetic

siblings where one was adopted and the other was reared in their birth home. The relative advantages of adoptive homes have been extensively documented in earlier research as well as in EGDS. On average, adoptive homes are characterized by greater material resources, lower parental psychopathology, increased marital stability and educational advantages as compared to non-adoptive homes. While it would be wrong to consequently idealize adoptive rearing as well as fail to recognize that the birth mother's circumstances can change and improve over time, it is likely that the adopted siblings will have been reared on average in more advantaged homes than their non-adopted siblings, so that the comparison between the two can provide useful information on the impact of what is analogous to a massive psychological intervention.

Ultimately, EGDS researchers seek to use findings from behavior genetic research to inform prevention and intervention efforts, a longstanding and commendable interest of members of the EGDS team. Two translational applications are envisioned. The first involves using EGDS to identify the actual familial causes of both adaptive and maladaptive child development. These in turn could be targeted in intervention/prevention trials. For the reasons outlined above, EGDS should have considerable utility in addressing this first translational aim. The second aim seeks to improve intervention efficacy by using findings from studies like EGDS to tailor treatments to participants' genetic backgrounds. This aim is premised on the assumption that individuals with differing genetic backgrounds will respond in different ways to various environmental interventions (i.e., gene-environment interaction). The prospect of precision medicine, and its derivatives precision psychiatry and even precision education, has been greeted with considerable enthusiasm (Sullivan et al., 2018). Yet to date, aside from in the treatment of cancer, the number of successful applications of genomic approaches to precision medicine has been limited and, in the case of behavior, arguably non-existent. The challenges to precision medicine approaches to behavioral intervention/prevention are primarily technical, giving hope they might be surmountable. The gene-environment interactions upon which precision approaches ultimately rest have been difficult to reliably establish for behavior even though their existence is assumed to be ubiquitous, according to developmental scientists (Halldorsdottir & Binder, 2017). Perhaps larger samples, along with rigorous assessment of exposure will prove more successful in establishing replicable interactions than previous attempts have been. Precision approaches will also depend on accurate methods for stratifying populations according to genetic risk. Currently, the standard approach to genetic risk stratification is to use polygenic scores (PGS), aggregate measures of genetic risk obtained by summing the effects of the numerous individual variants in the genome associated with any specific heritable phenotype. While the introduction of PGS represents an exciting development in the field, their currently modest predictive validity and lack of population generalizability limit their application as a basis for behavioral interventions (Martin et al., 2017). Although we remain optimistic, whether these technical issues can be overcome and truly individualized approaches to intervention/prevention achieved remains to be determined.

By advancing our understanding of the nature of gene-environment interplay in psychological development, EGDS is positioned to become one of the field's landmark studies from the early 21st century. This will not be because EGDS has completely solved the problem of confounding in family socialization research. No single study can. Indeed, the careers of the EGDS researchers have been marked by the use of multiple innovative research designs and statistical

analyses in order to engage the methodological triangulation that is needed for rigorous causal inference with observational data (Hammerton & Munafo, 2021). EGDS, and the careers of the EGDS principals, provide us with a model for how we can advance our understanding of the nature of psychological development through use of rich longitudinal data, innovative research designs, and incisive psychological theory.

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References

Bell, R. Q. (1968). A reinterpretation of the direction of effects in studies of socialization. *Psychological Review, 75*(2), 81-95. https://doi.org/10.1037/h0025583

Burks, B. S. (1927). Foster parent-foster child comparisons as evidence upon the nature-nurture problem. *Proceedings of the National Academy of Sciences of the United States of America, 13*(12), 846-848. https://doi.org/10.1073/pnas.13.12.846

Deneault, A.A., Hammond, S.I., Madigan, S. (2023). A meta-analysis of child–parent attachment in early childhood and prosociality. *Developmental Psychology, 59*(2), 236-255.

Foster, E.M. (2010). Causal inference and developmental psychology. *Developmental Psychology, 46*(6), 1454-1480. https://doi.org/10.1037/a0020204

Fraley, R.C., Roisman, G.I., & Haltigan, J.D. (2013). The legacy of early experiences in development: Formalizing alternative models of how early experiences are carried forward over time. *Developmental Psychology, 49*(1), 109-126. https://doi.org/10.1037/a0027852

Halldorsdottir, T. & Binder, E.B. (2017). Gene x environment interactions: From molecular mechanisms to behavior. *Annual Review of Psychology, 68*, 215-241.

Hammerton , G. L., & Munafò, M. R. (2021). Causal inference with observational data: The need for triangulation of evidence. *Psychological Medicine, 51*(4), 563-578. https://doi.org/10.1017/S0033291720005127

Kong, A., Thorleifsson, G., Frigge, M.L., Vihjalmssom B.V, Young, A.I., Thorgeirsson, T., . . . Stefansson, K. (2018). The nature of nurture: Effects of parental genotypes. *Science, 359*(6374), 424-428. https://doi.org/10.1126/science.aan6877

Leppert, B., Havdahl, A., Riglin, L., Jones, H. J., Zheng, J., Smith, G. D., . . . Stergiakouli, E. (2019). Association of maternal neurodevelopmental risk alleles with early-life exposures. *JAMA Psychiatry, 76*(8), 834-842. https://doi.org/10.1001/jamapsychiatry.2019.0774

Letcher, P., Greenwood, C.J., McAnally, H., Belsky, J., Macdonald, J.A., Spry, E.A., . . . Olsson, C.A. (2023). Parental history of positive development and child behavior in next generation offspring: A two-cohort intergenerational study. *Child Development, 94*(1),

60-73. https://doi.org/10.1111/cdev.13839

Lester, B.M., LaGasse, L. & Brunner, S. (1997). Data base of studies on prenatal cocaine exposure and child outcome. *Journal of Drug Issues, 27*(2),487-499.

Martin, A. R., Gignoux, C.R., Walters, R.K., Wojcik, G.L., Neale, B.M., Gravel, S., . . . Kenny, E.E. (2017). Human demographic history impacts genetic risk prediction across diverse populations. *American Journal of Human Genetics, 100*(4), 635-649. https://doi.org/10.1016/j.ajhg.2017.03.004

McCurdy, A.L., & Russell, S.T. (2023). Perceived parental social support and psychological control predict depressive symptoms for lesbian, gay, bisexual, transgender, queer, or questioning youth in the United States. *Child Development*, Early View, 1-15. https://doi.org/10.1111/cdev.13894

Plomin, R., & Bergeman, C. S. (1991). The nature of nurture: Genetic influence on environmental measures. *Behavioral and Brain Sciences, 14*(3): 373-385. https://doi.org/10.1017/S0140525X00070278

Raby, K.L., Roisman, G.I., Fraley, R.C., & Simpson, J.A. (2015). The enduring predictive significance of early sensitivity: Social and academic competence through age 32 years. *Child Development, 86*(3), 695-708. https://doi.org/10.1111/cdev.12325

Reiss, D., Ganiban, J. M., Leve, L. D., Neiderhiser, J. M., Shaw, D. S., & Natsuaki, M. N. (2023). Parenting in the Context of the Child: Genetic and Social Processes. *Monographs of the Society for Research in Child Development*, *87*(1-3). https://doi.org/10.1111/mono.12460

Rice, F., Lewis, G., Harold, G. T., & Thapar, A. (2013). Examining the role of passive gene–environment correlation in childhood depression using a novel genetically sensitive design. *Development and Psychopathology, 25*(Special Issue 01), 37-50. https://doi.org/10.1017/S0954579412000880

Rohrer, J.M., & Murayama, K. (2023). These are not the effects you are looking for: Causality and the within-/between-persons distinction in longitudinal data analysis. *Advances in Methods and Practices in Psychological Science, 6*(1): 1-14. https://doi.org/10.1177/25152459221140842

Rutter, M. (2007). Proceeding from observed correlation to causal inference: The use of natural experiments. *Perspectives on Psychological Science, 2*(4): 377-395.

Sasser, J., Waddell, J.T., & Doane, L. D. (2023). Family dynamics and adjustment across Latino/a students' transition to college: Disentangling within- and between-person reciprocal associations. *Developmental Psychology, 59*(3), 487-502. https://doi.org/10.1037/dev0001474

Sorjonen, K., Falkstedt, D., Wallin, A.S., Melin, B., & Nilsonne, G. (2021). Dangers of residual

confounding: A cautionary tale featuring cognitive ability, socioeconomic background, and education. *BMC Psychology*, 9, Article 145.

Sullivan, P.F., Agrawal, A., Bulik, C.M., Andreassen, O.A., Borglum, A.D., Breen, G., . . . Gelernter, J. (2018). Psychiatric genomics: An update and an agenda. *American Journal of Psychiatry, 175*(1), 15-27. https://doi.org/10.1176/appi.ajp.2017.17030283

Yang, P., Schlomer, G.L., & Lippold, M.A. (2023). Mothering versus fathering? Positive parenting versus negative parenting? Their relative importance in predicting adolescent aggressive behavior: A longitudinal comparison. *Developmental Psychology, 59*(1), 69-83. https://doi.org/10.1037/dev0001442