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Editorial

Epigenetics and behavioral development

1. Epigenetics and behavioral development

The time would seem to be right for a special issue of *Infant Behavior and Development* devoted to epigenetic contributions to behavioral development in infancy. Interest in epigenetics has grown dramatically in the last two decades; in merely the first 8 years of the 21st century, the word "epigenetics" appeared in books *six times* more frequently than it had appeared in the 50 years ending in 1999 (Moore, 2017b). The explosion of new science in this domain has led some journalists to conclude that "epigenetics" is now a "buzzword" (Park, 2015; Rutherford, 2015). But while intense interest in (and in some cases, speculation about) these ideas has led some writers to label epigenetics a "fad" (Ptashne, 2013; Shulevitz, 2012), research on how genetic activity is regulated by factors other than DNA continues to be published at an ever-increasing pace. There is little reason, therefore, to think interest in these developmental phenomena will be waning anytime soon.

2. Background & historical context

First, we place this work in context. Across hundreds of years, the word "epigenetic" has been, and continues to be, defined in several ways (Henikoff & Greally, 2016; Richards, Bossdorf, & Pigliucci, 2010); yet only recently has this word come to be associated with the idea of dynamic regulation of the activity of DNA. Historically, some philosophers recognized "epigenetic" as an adjective related to the word "epigenesis," referring to Aristotle's theory that biological development involves the emergence of structure from previously undifferentiated tissues (Aristotle, 1984). Although the epigenetic nature of development has been acknowledged for at least the last 100 years, this perspective has not always been embraced. During the 17th century, for example, the physician William Harvey argued against Aristotle's view of epigenesis by claiming that a whole, preformed animal can be found in an egg (Willis, 1847). A short time later in the 17th century, Atonie van Leeuwenhoek, using one of his early microscopes (Lane, 2015), also argued against an epigenetic nature of development by observing "that the denser substance of semen was seen to be made up of all manner of great and small vessels, so various and so numerous that I misdoubt me not that they be nerves, arteries, and veins. . . And when I saw them, I felt convinced that, in no full-grown body, are there any vessels which may not be found likewise in sound semen" (Wilson, 1995 p. 132). Similar preformationist ideas were even championed in the germ plasm theory put forth by German biologist August Weismann in 1894. Nevertheless, and around the same time as Weismann's germ plasm theory, Hans Driesch used two-cell sea urchin embryos to demonstrate that each of the cells could, and did, develop into separate, complete sea urchins. In other words, Driesch demonstrated that the original egg or sperm cell did not contain a single organism, or any other organ, as advocated by various preformationist thinkers such as Harvey and van Leeuwenhoek; instead, Driesch's result indicated that each organ and organism must be *built* in a dynamic developmental process that is context-dependent (see Moore, 2002 for a detailed review). Thus, and roughly since the time of Driesch in the late 19th century, epigenetic perspectives have steadily grown in their influence within the developmental sciences.

In the 1940s, the developmental biologist Conrad Waddington chose to use the word "epigenetics" to refer to what would become a new branch of biology devoted to studying how organisms' characteristics, or phenotypes, are brought into being via interactions that occur during development between genes and their cellular/nuclear contexts (Moore, 2013; Waddington, 1957, 1968). One of Waddington's significant contributions to thinking in this area is the idea of *canalization*, a word he coined in 1942 to refer to the buffering process by which organisms of a given species can develop a specific phenotype even when there is significant variation across their developmental environments. Waddington's original conceptualization of both canalization and epigenetics was rather biologically oriented (Hall, 1999), but toward the end of the 20th century, the developmental psychobiologist Gilbert Gottlieb (1991, 2007) conceived of a more experientially oriented way to think about development. According to Gottlieb's theory of "probabilistic epigenesis" (2007), there are dynamic and bidirectional influences within, and between, genetic, neural, behavioral, and

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environmental levels, which work together to cause—and in some cases, to canalize—development. In other words, while genes are important, they are only one level of developmental influence and are not unaffected by influences from other levels; instead, they "are in fact dependent on the other levels for initiating and terminating their activity" (Gottlieb, 2007, p. 2). In this sense, then, all developmental processes are epigenetic.

More recently, other theorists have argued that "epigenetics" should be understood to refer specifically to how gene expression changes as development proceeds (Jablonka & Lamb, 2002; Richards, 2006). While the term "epigenetics" has certainly evolved over time, the common element in these late 20th and early 21st century conceptualizations is *development!* Specifically, epigenetic processes are recognized to be integral and dynamic components of developmental processes because their involvement in genetic regulation inseparably connects them to the developmental events that build our phenotypes (Moore, 2015, 2017a).

We are most fortunate in that a substantial amount of research related to epigenetics has been done on medical conditions ranging from cancer (Feinberg, Ohlsson, & Henikoff, 2006; Feinberg, 2007) to diabetes (Bernal & Jirtle, 2010; Gluckman, Hanson, & Beedle, 2007) to the process of aging itself (Bjornsson et al., 2008). However, for behavioral scientists, the real excitement about epigenetics has been about the discovery that our experiences as we develop and interact with our environment influence the functioning of our DNA in ways that affect our behaviors, cognitions, and emotions. The branch of epigenetics that examines these effects on behavior has been called "behavioral epigenetics" (Miller, 2010; Moore, 2015, 2017a), and it continues to draw the attention of psychologists, particularly those associated with the developmental sciences. The publication in the last few years of special issues on epigenetics and gene-environment interactions in *Child Development* (January 2016), *Human Development* (September 2017), and *Research in Developmental Disabilities* (November 2018), for example, attests to ongoing interest in this field.

3. Introduction to the special issue

Consequently, a journal like *Infant Behavior and Development,* with its clear focus on early behavior and development, would seem to be an obvious home for a collection of papers on this emerging discipline. When we agreed to serve as Guest Editors of the journal's special issue on Epigenetics and Behavioral Development, we expected to receive a fairly large number of submissions. In the end, we received a small number of manuscripts, and, after the peer review process, we present a special issue with only two papers. Both are empirical reports—one is by Gui and colleagues (this issue) and the other is by Doherty, Bozeman, Roth, and Brumley (this issue)—and both will be briefly summarized below.

Although it is difficult to know why more papers were not submitted for this special issue, we can offer some speculation. One possibility is that epigenetics is such a hot topic that the competition for good papers has become quite stiff; it might be that there are a number of journals seeking to publish the results of studies of epigenetics. A related possibility is that scholars in possession of interesting behavioral epigenetics data would sooner submit their reports to journals targeting biologists than behavioral scientists. After all, as Buklijas (2018) noted, "epigeneticists, by and large, do not read social science research" (p. 168). A third possibility is related to the fact that many of the most compelling experiments in behavioral epigenetics (e.g., Day & Sweatt, 2010; Tung et al., 2012; Weaver et al., 2004) have been conducted on non-human animals, because such populations permit scientists to examine DNA in cell types that are likely to be affected by experiences but that cannot be accessed in healthy human beings (e.g., neurons in the brain). This constraint might be reducing behavioral epigenetics research on human populations, which has traditionally been the population of interest to readers of this journal. Finally, despite the excitement that this field has engendered in some quarters, it remains a relatively new area of study, with perhaps a relatively small number of researchers actually conducting the empirical investigations.

Regardless, there can be little doubt that additional work on how neural, behavioral, and environmental experiences influence gene expression will be illuminating, as will work on how these effects influence later behavioral phenotypes. In fact, we are confident that explorations of behavioral epigenetics, whether they are conducted on human or non-human populations, will have valuable implications for furthering our understanding of developmental processes *in general*. Even though important new papers on behavioral epigenetics continue to be published at a reasonable rate (e.g., Krol, Moulder, Lillard, Grossmann, & Connelly, 2019, Krol, Puglia, Morris, Connelly, & Grossmann, 2019; Perkeybile et al., 2018; Weinstein-Fudim et al., 2019), more studies are clearly needed, and insights gleaned from these efforts need to be shared with the broader developmental science community.

4. The current issue

Fortunately, fruitful paths forward for behavioral epigenetics can be found in the papers constituting this special issue. The two papers, respectively, provide thought-provoking revelations about how epigenetic factors could be involved in the development of Autism Spectrum Disorder (ASD; Gui and colleagues (this issue)) and motor behaviors (Doherty et al., this issue). Together, the contributions encourage further exploration by identifying both questions and methods likely to open new vistas in behavioral epigenetics.

The paper by Doherty et al. (this issue), explores mechanisms of plasticity in the central nervous system. Specifically, it reports on epigenetic alterations in the spinal cord that occur in response to an extreme developmental perturbation: spinal cord transection. Working with a population of infant rats, these experimenters tested the hypothesis that epigenetic factors in the developing spinal cord influence the considerable plasticity present in these tissues early in development. Their data supported this hypothesis, revealing "sweeping epigenetic changes in response to the developmental perturbation" and suggesting that "epigenetic alterations are prime candidates in the search for mechanisms underlying spinal cord development and associated behavioral trajectories."

The paper by Gui and colleagues (this issue) demonstrates how researchers can incorporate epigenetic data into prospective, longitudinal interrogations of the mechanisms underlying atypical behavioral development. Using epigenetic, behavioral, electrophysiological, parent-report, and diagnostic data collected on a small sample of infants evaluated at 8, 15, 25, and 36 months of age, these researchers conducted multiple exploratory analyses, including these three: an analysis that examined global DNA methylation in buccal epithelial cells and its relation to five later-emerging phenotypes, an analysis that measured relations between epigenetic changes and behavioral changes over developmental time, and an epigenome-wide association analysis. By identifying four types of effects that could be scrutinized productively in the future, Gui and colleagues alert readers to tools and conceptualizations that will be able to guide forthcoming prospective, longitudinal studies of human development in infancy.

5. Conclusion

Together, the papers in this special issue highlight both the challenges and rewards of studying the epigenetic phenomena associated with behavioral development in infancy. In the case of the articles presented herein, the authors' pioneering efforts will undoubtedly facilitate new discoveries in this domain. We began this editorial by stating that the time would seem to be right for a special issue showcasing recent inquiries into epigenetics and behavioral development, and we stand by that statement, notwithstanding the small size of this special issue. Furthermore, we remain sanguine about the potential of research on behavioral epigenetics to continue to uncover significant truths about development – including human development. We encourage this journal's readers and contributors to consider how new knowledge from the broad field of epigenetics, and behavioral epigenetics more specifically, can inform and extend their own work. Furthermore, we encourage behavioral epigeneticists to continue to discuss their findings within the context of developmental processes and to disseminate their findings across a broad range of developmental science literatures. Finally, we thank each of the contributors to this informative and insightful special issue on epigenetics and behavioral development.

Declaration of Competing Interest

The authors declare that they have no conflicts of interest.

References

Aristotle (1984). In J. Barnes (Ed.). *The complete works of Aristotle, the revised Oxford translations (Vol. 1)*. Princeton, NJ: Princeton University Press.
Bernal, A. J., & Jirtle, R. L. (2010). Epigenomic disruption: The effects of early develop mental exposures. *Birth Defects Research Part A, Clinical and Molecular Teratology, 88*, 938–944.
Bjornsson, H. T., Sigurdsson, M. I., Fallin, M. D., Irizarry, R. A., Aspelund, T., Cui, H., ... Feinberg, A. P. (2008). Intra-individual change over time in DNA methylation with familial clustering. *Journal of the American Medical Association, 299*, 2877–2883.
Buklijas, T. (2018). Histories and meanings of epigenetics. In M. Meloni, J. Cromby, D. Fitzgerald, & S. Lloyd (Eds.). *The palgrave handbook of biology and society* (pp. 167–187). London: Palgrave Macmillan.
Day, J. J., & Sweatt, J. D. (2010). DNA methylation and memory formation. *Nature Neuroscience, 13*, 1319–1323.
Doherty, T. S., Bozeman, A. L., Roth, T. L., & Brumley, M. R. (this issue). DNA methylation and behavioral changes induced by neonatal spinal transection. Infant Behavior and Development.
Feinberg, A. P. (2007). Phenotypic plasticity and the epigenetics of human disease. *Nature, 447*, 433–440.
Feinberg, A. P., Ohlsson, R., & Henikoff, S. (2006). The epigenetic progenitor origin of human cancer. *Nature Reviews Genetics, 7*, 21–33.
Gluckman, P. D., Hanson, M. A., & Beedle, A. S. (2007). Non-genomic transgenerational inheritance of disease risk. *BioEssays, 29*, 145–154.
Gottlieb, G. (1991). Experiential canalization of behavioral development: Theory. *Developmental Psychology, 27*, 4–13.
Gottlieb, G. (2007). Probabilistic epigenesis. *Developmental Science, 10*, 1–11.
Gui, A., Jones, E. J. H., Wong, C. C. Y., Meaburn, E., Xia, B., Pasco, G., … the BASIS Team (this issue). Leveraging epigenetics to examine differences in developmental trajectories of social attention: A proof-of-principle study of DNA methylation in infants with an older sibling with autism. Infant Behavior and Development.
Hall, B. K. (1999). *Evolutionary developmental biology (2nd Ed.)*. Dordrecht: Kluwer.
Henikoff, S., & Greally, J. M. (2016). Epigenetics, cellular memory and gene regulation. *Current Biology, 26*, R644–R648.
Jablonka, E., & Lamb, M. J. (2002). The changing concept of epigenetics. *Annals of the New York Academy of Science, 981*, 82–96.
Krol, K. M., Moulder, R. G., Lillard, T. S., Grossmann, T., & Connelly, J. J. (2019). Epigenetic dynamics in infancy and the impact of maternal engagement. *Science Advances, 5*, eaay0680.
Krol, K. M., Puglia, M. H., Morris, J. P., Connelly, J. J., & Grossmann, T. (2019). Epigenetic modification of the oxytocin receptor gene is associated with emotion processing in the infant brain. *Developmental Cognitive Neuroscience, 37*. https://doi.org/10.1016/j.dcn.2019.100648.
Lane, N. (2015). The unseen world: Reflections on Leeuwenhoek (1677) "concerning little animals.". *Philosophical Transactions of the Royal Society B: Biological Sciences, 370*, 1–10. https://doi.org/10.1098/rstb.2014.0344.
Miller, G. (2010). The seductive allure of behavioral epigenetics. *Science, 329*, 24–27.
Moore, D. S. (2002). *The dependent gene: The fallacy of nature vs. nurture.* New York: W.H. Freeman.
Moore, D. S. (2013). Behavioral genetics, genetics, & epigenetics. In P. D. Zelazo (Ed.). *Oxford handbook of developmental psychology* (pp. 91–128). New York: Oxford University Press.
Moore, D. S. (2015). *The developing genome: An introduction to behavioral epigenetics.* New York: Oxford University Press.
Moore, D. S. (2017a). Behavioral epigenetics. *WIREs Systems Biology and Medicine, 9*. https://doi.org/10.1002/wsbm.1333.
Moore, D. S. (2017b). The potential of epigenetics research to transform conceptions of phenotype development. *Human Development, 60*, 69–80.
Park, A. (2015, June 8). Explaining "epigenetics": The health buzzword you need to know. http://time.com/3911161/explaining-epigenetics-the-health-buzzword-you-need-to-know/.
Perkeybile, A. M., Carter, C. S., Wroblewski, K. L., Puglia, M. H., Kenkel, W. M., Lillard, T. S., ... Connelly, J. J. (2018). Early nurture epigenetically tunes the oxytocin receptor. *Psychoneuroendocrinology, 99*, 128–136.
Ptashne, M. (2013). Faddish stuff: Epigenetics and the inheritance of acquired characteristics. *The FASEB Journal, 27*, 1–2.
Richards, E. J. (2006). Inherited epigenetic variation—Revisiting soft inheritance. *Nature Reviews Genetics, 7*, 395–401.
Richards, C. L., Bossdorf, O., & Pigliucci, M. (2010). What role does heritable epigenetic variation play in phenotypic evolution? *BioScience, 60*, 232–237.
Rutherford, A. (2015, July 19). Beware the pseudo gene genies. https://www.theguardian.com/science/2015/jul/19/epigenetics-dna-darwin-adam-rutherford.
Shulevitz, J. (2012, September 8). Why fathers really matter. New York Times. Retrieved from https://nyti.ms/QavdtZ.

Tung, J., Barreiro, L. B., Johnson, Z. P., Hansen, K. D., Michopoulos, V., Toufexis, D., ... Gilad, Y. (2012). Social environment is associated with gene regulatory variation in the rhesus macaque immune system. *Proceedings of the National Academy of Sciences USA, 109*, 6490–6495.
Waddington, C. H. (1957). *The strategy of the genes.* London: Allen & Unwin.
Waddington, C. H. (1968). The basic ideas of biology. In C. H. Waddington (Ed.). *Towards a theoretical biology (vol. 1: Prolegomena, pp. 1–32).* (pp. 9–10). Edinburgh: Edinburgh University Press.
Weaver, I. C. G., Cervoni, N., Champagne, F. A., D'Alessio, A. C., Sharma, S., Seckl, J. R., ... Meaney, M. J. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience, 7*, 847–854.
Weinstein-Fudim, L., Ergaz, Z., Turgeman, G., Yanai, J., Szyf, M., & Ornoy, A. (2019). Gender related changes in gene expression induced by valproic acid in a mouse model of autism and the correction by S-adenosyl methionine. Does it explain the gender diff ;erences in autistic like behavior? *International Journal of Molecular Sciences, 20*. https://doi.org/10.3390/ijms20215278.
Weismann, A. (1894). *The effect of external influences upon development.* London: Frowde.
Willis, R. (1847). *The works of William Harvey, M.D.: On animal generation.* London: Sydenham Society.
Wilson, C. (1995). *The invisible world: Early modern philosophy and the invention of the microscope.* Princeton, NJ: Princeton University Press.

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