

PERSPECTIVES

The public reception of putative epigenetic mechanisms in the transgenerational effects of trauma

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Abstract

There has been great interest in the possibility that effects of trauma might be passed from parent to offspring through epigenetic mechanisms. This topic has stimulated discussion and controversy in the scientific literature, the popular press, and culture at large. This article describes the initial observations that have led to recent examinations of epigenetic mechanisms in association with effects of parental trauma exposure on offspring. Epigenetic research in animals has provided models for how such effects might be transmitted. However, the attribution of any specific epigenetic mechanisms in human studies of offspring of trauma survivors is premature at this time. The article describes some of the ways in which initial epigenetic findings in the offspring of trauma survivors have been represented in the popular media. Reports have ranged from overly simplistic and sensationalistic claims to global dismissals. The authors discuss the importance of clarity in language when describing epigenetic findings for lay audiences, the need to emphasize the limitations as well as the promise of research on intergenerational transmission of trauma effects, and the importance of countering popular interpretations that imply a reductionist biological determinism. Scientists have an obligation to assist in translating important research findings and nascent avenues of research to the public. It is important to recognize the ways in which this research may unintentionally be received as supporting a narrative of permanent and significant damage in offspring, rather than contributing to discussions of potential resilience, adaptability, and mutability in biological systems affected by stress.

Key words: intergenerational; epigenetics; PTSD; resilience; glucocorticoids; trauma; Holocaust

The Transformative Nature of Trauma

People surviving extreme adversity often describe feeling ‘transformed’ by those experiences. It is not uncommon to hear a trauma survivor state: “I’m not the same person I used to be,” regarding the effects of trauma exposure. This embodied experience of trauma has been supported by research documenting that many biological systems are affected by stress exposure, and implicated in posttraumatic stress disorder (PTSD). Long-term biological alterations associated with trauma have been observed in brain neurocircuitry, the hypothalamic-pituitary-

adrenal (HPA) axis, the sympathetic nervous system (SNS), and the immune system (reviewed in [1–3]). The idea that profoundly life-altering experiences can result in enduring and fundamental change, rather than just transient ones, was the core driver of the diagnosis of PTSD in 1980 [4].

The concept that stress effects could be longlasting was, at first, difficult to grasp since the essential paradigm governing an understanding of the body’s stress response generally emphasized acute, short-lived responses—such as those associated with “fight-or-flight.” After this, organisms, including people, recover, at least from the initial wave of arousal

when the threat has passed. Eventually, scientific research corroborated the notion of longlasting change by demonstrating unique biological alterations in association with chronic PTSD [5–7]. Molecular and epigenetic alterations in association with PTSD seemed particularly relevant to the subjective feeling that traumatic experiences create an indelible internal change [8–14]. As one Holocaust survivor described it “I don’t live in the past, the past lives in me.”

Persistence of Effects of Trauma into the Next Generation

A question that has arisen in parallel with the recognition of the long-term and transformative nature of the response to adversity is whether and to what extent offspring of trauma survivors are also affected biologically and/or psychologically by trauma exposure in their parents. If they are affected, what are the mechanisms through which these effects occur? Although on the most basic level, children will likely react to the trauma survivor’s narrative and altered behavior, a social learning model positing behavioral responses to a parent does not seem to adequately capture the extent to which the traumatic experiences of a parent permeates the life of a child. It is perhaps for this reason that there is so much excitement about the idea that effects of a parental trauma could persist into the next generation though epigenetic marks encoded on DNA and passed through the germ line. Even if epigenetic effects in offspring reflect their own biological accommodations to the parent, this would still be an indication of the power of the parental experience of trauma. If there is concrete biological representation of this, particularly involving the DNA, the societal conversation about the effects of trauma, and about the importance of prevention and treatment, changes. This commentary focuses on how this possibility has been represented in the popular press, and why a biological change involving marks on the DNA has such extraordinary resonance.

Origin of the Concept of Intergenerational Trauma in Modern Times

It is of interest to note that discussions about putative intergenerational effects of trauma predated the establishment of the PTSD diagnosis, and began with observations of the impact of the Holocaust on the children of its survivors in the mid-1960’s. In parallel with the developing concept of PTSD, the compelling nature of the clinical syndrome created a reality that was only later substantiated with biological data. Here too, as with PTSD, the first paper about intergenerational effects contained clinical anecdotal reports that Holocaust offspring seemed so affected by the trauma of the Holocaust that it was as if they themselves had been exposed [15]. At the time of this description, there were no known biological mechanisms (other than learning theory) that could explain these observations. Indeed, initial explanations for this phenomenon were psychodynamic. The suggestion that offspring might be affected by their parents’ experiences of trauma generated hundreds of publications on the topic, as well as considerable debate about whether there was or was not a uniform set of reactions to parental trauma exposure [16, 17]. To the extent that there were effects, the explanations for these effects were embedded within the disciplines of social psychology and family systems [18–21], but decidedly not biology.

The suggestion that offspring might be affected by their parents’ experiences of trauma continues to be somewhat of a lightning rod, despite its growing support in the academic

literature and popularity in the lay press. It is easy to see why the idea of transmitted effects of trauma might elicit a wide range of reactions. Certainly the possibility that trauma effects in parents could linger in offspring is potentially stigmatizing and victimizing, suggesting that offspring are somehow damaged or vulnerable as a result of preconception parental trauma. With respect to the Holocaust, which provided a substrate for the initial characterization of offspring effects, it is not difficult to imagine that many survivors wanted to demonstrate that the Nazis had failed in their stated mission of destroying Jews, not that they had bequeathed an ongoing legacy of vulnerability, damage or pain. The cultural narrative after the Holocaust was one of survival and resilience against all odds. If offspring were suffering as a result of their parents’ experiences, this might also imply blame or criticism of Holocaust survivors’ parenting or coping, a blaming of the victims that felt abhorrent. On the other hand, it is also easy to imagine that for some offspring who suffered greatly from the scars of their parents, documentation of intergenerational effects might be validating of their experiences. What has been remarkable to witness in the last few years is that the introduction of a scientific framework provided by the field of epigenetics and biological studies of offspring of trauma exposed parents (e.g. [22]) has not resolved prior debates on the nature of intergenerational effects of trauma, but rather has intensified them and created a larger urgency to understand such effects and if warranted, reverse them.

Transmission of Effects to Offspring as a Form of Biological Learning

One of the consequences of severe adversity is learning. It is not surprising that a traumatized parent would wittingly or unwittingly pass on the lessons and knowledge gleaned from traumatic experiences to their children. It is not always in the power of the parent to control the message, nor is the child a passive vessel for receiving parental effects. However, learning, especially in the context of fear-potential, involves molecular process [23–27]. If traumatic events occurring prior to conception are somehow encoded in the parent, this may shape biological predispositions in the offspring whether because of epigenetic changes in germ cells evident at conception, changes occurring as a result of prenatal contributions of an anxious or symptomatic mother, or because the symptoms of trauma affect postnatal attachment and parenting. The notion that trauma effects may reach into subsequent generations also points to the possibility of resilience, flexibility, and wisdom in survivors’ offspring, not just vulnerability and damage. Regardless of the interpretation of such effects, that offspring are affected by adverse exposures of their parents—or more accurately, by the effects of trauma on their parent—does not stretch the imagination. However, to date, it has not been possible to validate models of potential non-genomic (epigenetic) heritability, except, possibly in animal models.

The literature on intergenerational effects of trauma is no longer confined to studies of Holocaust offspring, and evidence of such effects has been reported in multiple cultures, societies and collective traumatic exposures [28–31]. These descriptions are predominantly in association with experiences involving subjugation of one people by another, as in racism, genocide, and war. The impact of these communal traumas goes beyond individual experiences of parent to offspring influences, because the impact of widespread atrocity shapes the collective experience of an entire generation, fundamentally altering the

fabric of culture and society. The more nuanced question is not whether offspring are affected by parental trauma, but which offspring are affected and how. If there are universal effects of parental trauma on offspring, it would be important to elucidate a mechanism explaining such effects. If there are cultural and social mediators, or even individual differences among trauma survivors and their offspring, these findings as well, would be important to understand.

Individual Differences in Offspring Effects

Two comprehensive reviews [16, 17] reported that in non-clinical populations, offspring of Holocaust survivors did not demonstrate higher rates of psychopathology. However, the studies summarized in these reviews assessed offspring without consideration of parental symptoms. When parental PTSD status was assessed, it became clear that Holocaust offspring demonstrated higher rates of PTSD in association with maternal PTSD, and higher rates of mood and anxiety disorders in association with PTSD in either parent [32]. This finding is critical to an understanding of what, in essence, is affecting the offspring. It may not be trauma exposure alone, but the persistence of enduring and disabling effects of the exposure (such as in PTSD) in a subset of survivors that is associated with offspring effects.

Understanding that trauma-induced parental symptoms may mediate—perhaps in ways that are sex-specific—the offspring phenotype, also in ways that might be sex specific, provides a context for examining individual differences in offspring responses. The elucidation of contributors to individual differences in offspring effects may in turn address areas of contention or disagreement about such effects. One area in particular that may become increasingly relevant to understanding individual differences in offspring effects concerns the period in development at which the parent was exposed—early childhood (preuberty) vs. adulthood, and the interval between exposure and conception of the offspring [33–35]. Different epigenetic mechanisms will certainly be operational in relation to these considerations.

Biological Studies in Offspring of Trauma Survivors

Initial findings of neuroendocrine alterations in Holocaust offspring supported a role for parental PTSD in mediating offspring effects, and in fact demonstrated distinct biological alterations in offspring in association with maternal vs. paternal PTSD. Prior to examining offspring effects by parental gender, initial studies demonstrated that Holocaust offspring exhibited alterations in many of the same neuroendocrine markers as individuals with PTSD, even in the absence of a history of their own trauma [36]. Many of the offsprings recruited in these studies were raised by two Holocaust parents. It was only because of an emerging literature indicating the importance of the in utero environment to offspring effects, as well as our own observations, that our studies began to focus on offspring effects based on parental gender [37–41].

The most important finding from biological studies of Holocaust offspring was that most effects were mediated by parental PTSD in response to parental Holocaust exposure. Compared with controls, Holocaust offspring of parents with presumptive PTSD demonstrated lower urinary and plasma cortisol levels and greater glucocorticoid sensitivity [42–45]. A later study clarified that offspring of mothers with PTSD tended to

demonstrate the above findings of lower cortisol levels and greater glucocorticoid receptor sensitivity whereas offspring with fathers, but not mothers, with PTSD tended to exhibit elevated cortisol levels and show evidence of lower glucocorticoid receptor sensitivity similar to what has been described in major depressive disorder [46]. Even in the absence of epigenetic findings, the clinical and neuroendocrine data presented a very clear picture that offspring of Holocaust survivors with PTSD were both psychologically and biologically affected by their parents' experiences. Interestingly, however, the introduction of putative biological markers of parental trauma effects (e.g., PTSD) did not generate much controversy or attention in either the scientific or popular press.

Epigenetic Findings in Holocaust Offspring

Twenty years after publication of our initial findings of neuroendocrine alterations of the HPA axis in offspring associated with parental PTSD, epigenetic tools became available to measure methylation in blood cells. Our group, and others, began examining epigenetic marks relevant to glucocorticoid functioning in offspring of trauma survivors. In 2014, our group showed lower methylation at the glucocorticoid receptor gene (NR3C1) 1F promoter region in Holocaust offspring who had two parents or one mother with PTSD, consistent with enhanced glucocorticoid sensitivity [47]. Lower methylation was associated with greater cortisol suppression following the low dose dexamethasone suppression test, an indicator of glucocorticoid sensitivity. The findings were noteworthy for several reasons, not least of which was the observation that an epigenetic mark in the glucocorticoid receptor gene in a peripheral blood cell could be related to parental PTSD. In parallel with the endocrine findings above, in offspring with only fathers with PTSD, GR gene methylation was elevated. This was the first study to examine the effect on offspring methylation of a preconception trauma in mothers and fathers who both experienced the same trauma. The fact that Holocaust offspring were adults—some nearing middle age—suggested that the findings reflected an enduring biologic feature, but such conclusions can only be suggested, not proven, in cross-sectional research. A second study examined methylation of intron 7 of the FKBP5 gene, which encodes a protein for a co-chaperone of the bound cortisol glucocorticoid receptor complex, in a small and different sample of Holocaust survivors and their own children [48]. The findings showed alterations at the same site within intron 7 in both parents and their own children that were positively correlated, but directionally distinct (when compared to their respective control groups). These findings continue to represent the only epigenetic study of preconception parental trauma effects in both parents and adult children. Notably, the Holocaust, but not its psychobiological impact, had ended years prior to conception of the offspring.

In the scientific literature, epigenetic mechanisms through which environmental stimuli affect gene expression had previously been identified or implicated in several interesting paradigms. These include the effects of maternal behaviors in animals [49], intrauterine effects on the developing fetus [50], and more recently, intergenerational effects of pre-conception trauma in male sperm cells in animal models of early stress [51]. Such studies are reviewed in several recent publications [51–56]. As these observations from animals and humans have converged, a new dialogue has emerged, and with it a new challenge. Because there are now carefully elucidated mechanisms of transmission of trauma effects to the next generation in several animal models, this has created a fertile field for premature

attribution of similar mechanisms to the observations in Holocaust offspring and, potentially, other human samples. While this has primarily occurred in lay publications, the cultural narrative may very well have fed back to affect the scientific literature. In so doing, recent research on potential epigenetic marks associated with the intergenerational transmission of trauma has fueled both intense interest and controversy in the scientific and popular press.

Epigenetics in the Popular Press: Potential for Oversimplification and Overcorrection

Although research on intergenerational transmission of trauma effects via epigenetic mechanisms in people has only just begun, potential applications of this research does not seem to be lost on consumers. These include journalists, filmmakers, artists, policy makers, clinicians or even other scientists, some of whom have translated limited and preliminary findings into overarching assumptions about the ‘heritability’ of trauma exposures and its potential ramifications for individuals, society, and culture.

Scientific reports in peer-reviewed journals are charged with providing descriptions of the methods, including their limitations, findings, and the implications of the work. Most published research in a field reflects interim observations that are refined by subsequent observations. Research findings are often couched in tentative language, noting features of the study that may limit the interpretation or generalizability of findings. Responsible scientists call for replication and inquiry into areas not sufficiently addressed, and successful papers are those that in fact stimulate others to engage in replication, extension and refinement. Scientific “facts” are thus established by interlocking studies that provide convergent and redundant support for a hypothesis. Individual studies are links in a chain, sometimes pearls in a strand, and only rarely, a solitaire. In this way, the process of science is ultimately self-correcting, and fundamentally revisionist. This iterative process, subject to peer review, promotes creativity and risk, encourages the introduction of new ideas, and stimulates appropriate discussion. Scientific dialogue is sometimes sharply critical in content, but with a shared intent and goal of discovery. Scientists expect areas of disagreement and disparate findings until new data resolve them.

Science reporting by journalists is increasingly commonplace as scientific journals make outreach attempts through press releases to convey information to the lay public about important developments. The internet has increased the appetite of consumers for scientific knowledge, and journalists have an important role in translating the technical details and interpretation of scientific research into a relatively brief summary that can be understood by a lay audience. Inherent in this mandate is the potential for oversimplification, and for obscuring the boundary between hypothesis and fact. It may be challenging to convey enthusiasm for a potential new lead while providing the required cautionary note. Coverage of science or an attention getting headline can catapult even preliminary findings into the public eye, creating the appearance of more established fact than is warranted.

The simplification that is often necessary for good, clear journalism can foster inferences that go far beyond the original observation from which the inferences were drawn. This occurred in the coverage of the epigenetic findings regarding Holocaust offspring described above. For example, a 2016 article

in *Teen Vogue* (<https://www.teenvogue.com/story/slavery-trauma-inherited-genetics>) was titled, “Trauma from slavery can actually be passed down through your genes,” with the tag line “you can get PTSD from your ancestors.” This article described research findings published by our research group, but the author did not interview anyone from the team. The article stated that when people experience trauma it changes people’s genes “in a very specific and noticeable way” and that when traumatized parents have children “their genes are passed down to their children, [and] the children also inherit the genes affected by trauma.” A *Daily Beast* story (<https://www.thedailybeast.com/can-we-inherit-memories-of-the-holocaust-and-other-horrors>) asked “can we inherit memories of the Holocaust and other horrors?” The tagline stated that “descendants of victims of atrocities are inheriting those experiences in their DNA.” The *Epoch Times* (https://www.theepochtimes.com/children-of-genocide-survivors-can-inherit-trauma-in-their-dna_1910376.html) reported that “it is now scientifically proven that intergenerational trauma is not only passed on through sociocultural environments, but also through our DNA” and that “children of genocide survivors can inherit trauma in their DNA.” These articles raise the question of what could or should have been done differently either in the original writing of the peer-reviewed scientific paper, or in interviews that occurred or should have occurred thereafter. Importantly, the articles raise the question of how to carefully correct the record by offering more precise interpretations, without casting doubt on the actual observations or minimizing the potential relevance of the findings.

The idea that there are epigenetic influences on offspring of trauma survivors has begun to permeate popular culture, suggesting something deeply compelling about this narrative. References to epigenetic influences of parental trauma can be seen in art and entertainment. For example, the musical comedy-drama *Crazy Ex-Girlfriend* included a segment (Season 2, 2017) where the main character nods to epigenetics as she knowingly informs the rabbi, “Jewish people’s DNA is literally imprinted with our past trauma.” The popular Amazon show *Transparent* features an episode in Season 2 (2015) in which a character reads about epigenetics and inherited trauma and shares her findings with a friend: “do you know there is such a thing as inherited trauma?” The message of these journalistic and popular culture references to epigenetics appears to be one of predetermined damage that cannot be negotiated. Epigenetic changes may equally reflect the effects of parental trauma to increase the offspring’s ability to adapt to their environments, a key to achieving resilience.

In response to claims in the media such as those described in above, the *Chicago Tribune* (<http://www.chicagotribune.com/lifestyles/health/ct-holocaust-trauma-not-inherited-20170609-story.html>) published an article asking whether survivors of trauma will pass on their experiences to their children. Their conclusion was that a “close look at the research” indicates that “the answer so far is no.” An article in the *Dallas News* (<https://www.dallasnews.com/news/debunked/2017/05/30/trauma-inherited>) under the header “Debunked” is titled, “No, trauma is not inherited.” These reports often identify limitations of the research, such as sample size, which are typically discussed in the primary paper. However, such articles tend to present such limitations as if they had been exposed by the journalist, rather than by the authors themselves. Thus, what is in essence being debunked is not the original data, but a prior journalistic over-interpretation. In such articles, journalists may also ask another researcher to comment on the limitations

so as to create the impression that scientists like to debunk one another rather than to engage in a collaborative process of critique and correction to move the field forward. When a topic has social, cultural and political implications, there may be an underlying agenda of the reporting, such as, for example, to either negate or validate the influence of parental trauma on offspring.

After seeing the media coverage of our work, it is easy in hindsight to see how important it would have been to emphasize repeatedly that a change on the gene is not a change in the DNA itself, and that the functional impact of an alteration as a single epigenetic site could not be determined or even estimated on the basis of the correlational data presented. In retrospect, terms like “intergenerational transmission of trauma effects” which are used regularly in scientific journals, might convey mechanism even when used only to be descriptive. Such terminology leaves room for misinterpretation. Terms such as “inherited trauma” also obfuscate rather than clarify what is being transmitted and how—indeed, how can an experience be inherited? It is clearer to frame the discussion around how the *impact* of a trauma occurring to the parent can affect the offspring. Thus, the term “intergenerational trauma” is misleading because it is meant to refer to the intergenerational manifestation of the *effects* of parental trauma. The observation of biological marks in offspring associated with the impact of parental trauma is not an observation that trauma itself is transmitted, whatever that would mean. When discussing intergenerational research, it is imperative to be clear about what is being transmitted and whether the data illuminate potential mechanisms, or not.

Why Is Epigenetics so Powerful in the Popular Imagination?

The suggestion that epigenetic alterations associated with pre-conception trauma effects may be transmitted to offspring through germ cells raises the possibility of direct biological transmission of the effects of trauma. This possibility is different from the contribution of *in utero* effects on fetal development in that it represents a more purely biological transmission—unassociated with maternal state during gestation or later parenting influences that are potentially controlled and changeable. Such a consideration appears to have spurred the intense interest around epigenetic findings that eluded earlier findings of biological alterations in offspring associated with parental trauma and PTSD, raising the question of what it is about this potential mechanism that has so captured the popular imagination. In some ways, the presence of epigenetic marks associated with preconception parental trauma seems to imply a kind of blameless and predestined legacy. Perhaps the widespread reception of this research speaks to a cultural fear of powerlessness and lack of agency, or reflects a cultural moment in which objective evidence of a trauma-induced alteration seems to validate suffering that has been dismissed or trivialized. Regardless of the explanations for popular interest in the research, the determination that epigenetic mechanisms provide a potential vehicle for the intergenerational transmission of parental trauma effects does contribute meaningfully to the social and cultural narrative.

There appear to be two themes at play: the first, that effects of trauma may be biologically ‘transmitted’; the second, that such biological transmission can translate for some to a reductive stance that biology is destiny. It is the work of the scientific

community to challenge or refine these narratives. Epigenetic marks must be explained as potentially enduring but also malleable, rather than as a permanent alteration to offspring DNA. The functional relevance of any epigenetic mark requires much further study, and the distinction between statistically significant group differences in methylation levels, for example, and functionally relevant outcomes should be emphasized. The observation of epigenetic marks associated with parental trauma effects or PTSD opens the door to questions regarding the functions and consequences of these biological signatures but does not answer them. Lay interpretations that trauma cannot be overcome and damages offspring, or that its consequences leave little room for corrective environmental influences, choice, healing, or resilience must also be challenged. Even enduring marks exist within complex biological systems that have their own influences, calibration systems, and adaptive potential. The risk of popular dissemination of findings of epigenetic effects on offspring is that a story may be conveyed of permanent damage or defect over which offspring are powerless. The potential adaptiveness of epigenetic influences must be kept in the conversation, as such alterations may be an index of preparedness and are as likely to foster resilience as vulnerability. Moreover, the effect of observed epigenetic changes in offspring likely vary across the offspring’s lifespan, and may depend on environmental influences. The story of permanence also privileges one experience over others, failing to acknowledge that learning and experiences accrue over a lifetime. While the search for molecular mechanisms through which trauma influences individuals and their offspring is important, so too is an appreciation of the complexity of human experience and growth, that cannot be reduced to our DNA, or even the epigenome.

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