

Epigenetic Transmission of Holocaust Trauma: Can Nightmares Be Inherited?

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ABSTRACT

The Holocaust left its visible and invisible marks not only on the survivors, but also on their children. Instead of numbers tattooed on their forearms, however, they may have been marked epigenetically with a chemical coating upon their chromosomes, which would represent a kind of biological memory of what the parents experienced. As a result, some suffer from a general vulnerability to stress while others are more resilient. Previous research assumed that such transmission was caused by environmental factors, such as the parents' child-rearing behavior. New research, however, indicates that these transgenerational effects may have been also (epi)genetically transmitted to their children. Integrating both hereditary and environmental factors, epigenetics adds a new and more comprehensive psychobiological dimension to the explanation of transgenerational transmission of trauma. Specifically, epigenetics may explain why latent transmission becomes manifest under stress. A general theoretical overview of epigenetics and its relevance to research on trauma transmission is presented.

Some children of Holocaust survivors have terrible nightmares in which they are chased, persecuted, tortured or annihilated, as if they were re-living the Second World War over and over again. At these times, they suffer from debilitating anxiety and depression which reduce their ability to cope with stress and adversely impact their occupational and social function. It seems that these individuals, who are now adults, somehow have absorbed the repressed and insufficiently worked-through Holocaust trauma of their parents, as if they have actually *inherited the unconscious minds* of their parents.

Apparently, not only children of Holocaust survivors, but offspring of other PTSD parents are also vulnerable to such a burdensome legacy, including descendants of war veterans (1), survivors of war trauma and childhood sexual abuse, refugees, torture victims and many others (2). Moreover, the transmission may continue beyond the second generation and also include the grandchildren, great grandchildren and perhaps others as well. This process of *transgenerational transmission of trauma* (TTT) has been repeatedly described in the academic literature for more than half a century (3).

Generally speaking, TTT refers to the process in which a trauma that happened to the first generation was passed on to the second generation. Such a process is deeply connected with the general theme of *heredity* – the transmission of characteristics from parents to their offspring. Despite more than 500 studies published, however, we are still unable to sufficiently explain exactly *how* the *unconscious* trauma of a PTSD parent can be *genetically* transmitted to a child and to verify this idea with sufficient empirical evidence. Such a notion evades any simple and logical explanations. How can a repressed memory be passed on from one person to another? Can a child really “inherit” the unconscious mind of a parent? Is it possible for a child to remember what the parent has forgotten? Will we ever be able to produce “hard” neurobiological evidence of such far-fetched and preposterous assumptions and perhaps *see* traces of the unconscious trauma of a PTSD parent in a blood specimen or an MRI scan of the child? Probably not. But even though we still know very little about the level of specific inheritance of trauma, new research indicates that traumatic experiences of parents may indeed lead to a general disposition to PTSD in the offspring. Family and twin studies have found that risk for PTSD is associated with an underlying genetic vulnerability and that more than 30% of the variance associated with PTSD is related to a heritable component (4). Perhaps this heritable component can

be observed in the epigenetic marks that affect gene expression patterns in the nervous system?

Four major theoretical approaches to understanding trauma transmission have been earlier suggested by Kellermann (5): (1) psychodynamic relational models (6); (2) sociocultural and socialization models (7); (3) family systems and communication models; and (4) biological or genetic models. Children are of course influenced by their parents in a variety of ways, either through upbringing or heredity, or through both (8) and such an integrative view of trauma transmission seems to make perfect sense. Upon further inspection however, these theories are too *general* to sufficiently explain the *specific* process of how the impact of trauma can cross generations and how social and biological influences interact to produce TTT.

As emphasized by Jablonka and Lamb (9), genetic mechanisms alone cannot explain how some cellular traits are propagated and heritable changes in gene expression and regulation that have little to do with DNA sequence seem to be more relevant to explain TTT. Any theory explaining transgenerational transmission of trauma must therefore take into account the powerful *hereditary variations* which would explain how parental trauma may be biologically passed on to the child before birth. These theories should explain how children *who have not themselves been traumatized* tend to manifest inherited emotional problems.

Even though empirical data are still poor in comparison to the ideas presented here and my assumptions may sound bold, speculative and unfounded at this point in time, I suggest that epigenetics may introduce a promising new and more comprehensive explanatory variable of TTT than the earlier ones. Since it includes both hereditary and environmental factors, it may add a significant psychobiological dimension which could confirm clinical observations with empirical research. The purpose of this paper is therefore to explore what epigenetics can teach us about TTT and to review some of the prevalent empirical research in this field. Finally, I will show how the inclusion of epigenetics would explain some of the discrepant findings from previous research on the transgenerational transmission of Holocaust trauma.

EPIGENETIC TRANSMISSION

More than two centuries ago, the founder of evolution, Jean-Baptiste Lamarck, suggested that acquired characteristics may be transmitted from one generation to another. Ever since, evolutionary developmental biology

has continued to study this assumption. Recent advances in the field of *epigenetics* are now revealing a molecular basis for how heritable information other than DNA sequence can influence gene function (10, 11). These advances may add greatly to our understanding of trauma transmission and may even establish a promising new research paradigm in the field, as recently pointed out by Yehuda and Bierer (12): “Epigenetic modifications, such as DNA methylation, can occur in response to environmental influences to alter the functional expression of genes in an enduring and potentially, intergenerationally transmissible manner. As such, they may explain inter-individual variation, as well as the long-lasting effects of trauma exposure. Although there are currently no findings that suggest epigenetic modifications that are specific to posttraumatic stress disorder or PTSD risk, many recent observations are compatible with epigenetic explanations” (p. 427). Naturally, various questions remain regarding such assumptions, and we still know too little about where to draw the line between PTSD based on a single traumatic event, complex and chronic PTSD, as well as individuals who have largely overcome their responses to overwhelming stress.

Epigenetics is typically defined as the study of heritable changes in gene expression that are not due to changes in the underlying DNA sequence. Such heritable changes in gene expression often occur as a result of environmental stress or major emotional trauma and would then leave certain marks on the chemical coating, or *methylation*, of the chromosomes (13). The coating becomes a sort of “memory” of the cell and since all cells in our body carry this kind of memory, it becomes a constant physical reminder of past events, our own and those of our parents, grandparents and beyond. “The body keeps the score” (14), not only in the first generation of trauma survivors, but possibly also in subsequent ones. Because of their neurobiological susceptibility to stress, children of Holocaust survivors may thus easily imagine the physical suffering of their parents and almost “remember” the hunger, the frozen limbs, the smell of burned bodies and the sounds that made them scared.

In the same way as parents can pass on genetic characteristics to their children, they would also be able to pass on all kinds of “acquired” (or epigenetic) characteristics, especially if these were based on powerful life-threatening experiences, such as survival from starvation, torture or persecution. Such environmental conditions would leave an imprint on the genetic material in eggs and sperm and pass along new traits even in a single generation.

Such an explanation of TTT can be described in computer terminology in which the genome would represent a kind of hardware that remains fixed, while the *epigenome* would represent the variable software with all the memory files. The epigenome thus would function like a “switch,” which has the inherent ability to turn certain functions “on” or “off.” From such a point of view, offspring of trauma survivors would be somehow “programmed” to express a specific cognitive and emotional response in certain difficult situations. In effect, these children of PTSD parents would be suffering from a kind of “software bug,” an error in a computer program or system that produces incorrect or unexpected results, or causes it to behave irrationally. This bug would for example switch on a panic attack and instruct the genes to prepare for “fight and flight” when triggered, as if the individual were thrown into a Nazi persecution manuscript of catastrophic proportions, even in a relatively non-threatening situation. Metaphorically, such an epigenetic coating would affect the child of survivors in a way which is similar to a computer infected with a malicious *virus*, a malware that inflicts harm at certain unpredictable points in time.

Any such explanation in epigenetic terms of how the Holocaust trauma can “run in families” must first show that the PTSD parent was somehow “damaged” with some kind of brain short-circuit or constitutional “PTSD bug” and then demonstrate that the child was born with this same “bug.” Among children and grandchildren of Holocaust survivors as well as offspring of other traumatized populations, this “bug” would be manifested as a latent susceptibility to (secondary) PTSD and would cause increased vulnerability to stress under certain conditions, such as when a new stress becomes the trigger to a past traumatic event. At such times the epigenetic switch would turn the survival strategy “on” and activate a specific neuro-biological response. Initially, most affected offspring would not be aware of its origin or even of its existence until a new trauma occurs, and then be surprised that some old trauma of the parents would suddenly be surfacing.

If any *specific* past memory can be epigenetically transmitted or not, however, must be left open to speculation and we should be careful not to slip from reasonable assumptions to fantastic and unsupported scenarios. While a general tendency for having frightening nightmares may well be epigenetically transmitted, and the persecution nightmares of children of Holocaust survivors may be colored by their Holocaust imagery, we are obviously still unable to show that the content of a specific

nightmare is affected by epigenetic marks transmitted in a reproductive cell or in the womb. Eva Jablonka (personal communication) writes: “We have good reasons to believe that epigenetic marks can be inherited between generations, including marks that affect gene expression patterns in the nervous system. Of course, we need evidence that this actually happens in the case of human PTSD, but we do know that the effects of psychological stress are inherited in mice and rats. It would therefore not surprise me if we find out that the disposition to PTSD is inherited via an epigenetic route, and that traumatic experiences of parents lead to extra-sensitivity to traumatic inputs in offspring, and this may linger for some generations. If the effects of trauma are inherited we shall have to find out for how many generations (this may vary, depending on genetic background, type of trauma, and the persistence of traumatic experiences) and whether the effects make the descendants more prone to develop PTSD. Even if the disposition to develop PTSD is found to be increased in descendants, it is important to emphasize that the specific trauma is unlikely to be inherited. So the fact that children of Holocaust survivors dream of the Holocaust was not transmitted through gametic epigenetic inheritance (as a mark on the chromosomes of the parental sex cells). What could have been inherited is the disposition to have nightmares, and of course if they know something about the Holocaust through primary exposure, from stories and so on, the nightmares will take this form. What we know about epigenetic marks is that they can dispose one towards developing some behaviors, but the specific behavior depends on specific inputs the person gets in its own lifetime.”

EPIGENETIC RESEARCH

The field of epigenetics is becoming increasingly more accepted by the scientific community and there has been a large increase in studies conducted during the last decade. A comprehensive review of more than hundred studies of transgenerational epigenetic inheritance was compiled by Jablonka and Raz (15) who described the phenomena in a wide range of organisms, including bacteria, plants and animals. These studies included various kinds of adverse conditions, early stress and “emotional trauma” of the “first generation” which altered the gene expression in the subsequent generations. Reik, Dean and Walter (16) also reviewed what is known about reprogramming in mammals and discussed how it might relate to developmental potency and imprinting. More

recently, Franklin et al. (17) showed that chronic and unpredictable maternal separation induces depressive-like behaviors, not only in the first generation of mice, but also in their offspring. Empirical evidence of epigenetic transmission in human beings, however, is very scarce because of the difficulties in gathering relevant data from human as compared to animal subjects. Some of these will be summarized here briefly.

One of the first epigenetic studies on human beings was carried out by Bygren et al. (18) in Överkalix in Northern Sweden. He found that overeating as a youngster could initiate a biological chain of events that would lead one's grandchildren to die decades earlier than their peers did (19). Thus it was shown – perhaps for the first time – that a famine or overeating at critical times in the lives of the grandparents could influence the life expectancy of the grandchildren. In their efforts to replicate this astounding finding, Pembrey et al. (20) conducted another transgenerational study which showed that sons of men who smoke in pre-puberty were found to be at higher risk for obesity and other health problems than sons of non-smoking fathers. Much later, a series of unique post-mortem studies on the brains of men who had committed suicide in Canada (21) found that the chemical coating on genes seem to have been influenced by exposure to childhood abuse.

Additional indirect evidence came from the Dutch Famine Birth Cohort study (22) who concluded that exposure to acute, severe famine during pregnancy alters the distribution of birth weights of both the women born at the time of the famine and, through a phenotypic response, that of their own offspring. Even though it is clearly difficult to separate phenotypic (i.e., potentially modifiable) and genotypic (i.e., immutable) effects across generations, the complex mechanisms by which transgenerational transmission of stress responsiveness occur are rapidly becoming a focus of investigation (23). Rachel Yehuda and her team from the Mount Sinai School of Medicine have been at the forefront of this research for more than a decade (24). Having found that parental PTSD appeared to be a relevant risk factor for the development of PTSD in adult offspring of Holocaust survivors with PTSD, Yehuda and Bierer (25) summarized recent neuro-endocrine studies in offspring of parents with PTSD. These studies indicated that offspring of trauma survivors with PTSD had significantly lower urinary cortisol excretion and salivary cortisol levels as well as enhanced plasma cortisol suppression than offspring of survivors without PTSD. In all cases, neuro-endocrine

measures were negatively correlated with severity of parental PTSD symptoms, even after controlling for PTSD and other symptoms in offspring.

Though the majority of their work focused on adult offspring of Holocaust survivors, more recent observations in infants born to mothers who were pregnant on 9/11 demonstrated that low cortisol in relation to parental PTSD appears to be present early in the course of development and may be influenced by gluco-corticoid programming in unborn children. Lower cortisol levels were found in mothers who developed PTSD after exposure to the attacks on September 11 compared with similarly exposed mothers who did not develop PTSD (26). Pregnant women, who had been close to the World Trade Center on September 11th, 2001, gave birth to babies who had elevated levels of stress agents in their saliva (27-29). These data suggest that effects of maternal PTSD on cortisol can be observed very early in the life of the offspring and highlight the in utero effects as contributors to biological risk factor for PTSD (30). Since low cortisol levels are particularly associated with the presence of maternal PTSD, the findings suggested the involvement of epigenetic mechanisms. In a more recent study on combat war veterans with and without PTSD, this line of research was continued and the PTSD+ group again showed greater cortisol and ACTH suppression (31, 32).

In an early study of maternal Hypothalamic-Pituitary-Adrenal Axis (HPA-axis) functioning, Schechter et al. (33) measured maternal salivary cortisol within a clinical sample of mothers before and after a mother-child interaction protocol involving separations and reunions. The study showed modest, but significant associations between pre-separation cortisol as well as cortisol reactivity with the severity of maternal PTSD, dissociative symptoms, and atypical care giving behavior. Later studies of gene environment interactions focused on environmental stressors such as interpersonal violence and the regulatory effects of the serotonin transporter gene and other genes with which it is known to interact on the HPA axis (34).

Apparently, parenting itself may be epigenetically transmitted from parent to child. In a fascinating study of gene-environment interaction, Beaver and Belsky (35) recently found a significant interaction between parenting quality and cumulative genetic plasticity in the prediction of parental stress during adulthood. Depending on genotype, parenting quality was thus shown to differentially affect future parental stress. Exposure to maternal

parenting was measured prospectively when respondents were adolescents and parental stress was measured when they were parents themselves, some 14 years later. Some genes that seem to affect neural plasticity were shown to be involved and the variation in these genes affected parental behavior and the response to stressful parenting.

Finally, a range of different neurotransmitters have been investigated, from serotonin and dopamine to neuro-peptide Y, brain-derived neuro-trophic factor, and the gluco-corticoid receptor in the predisposition to PTSD. In their review of molecular genetic studies relating to PTSD, Broekman, Olff and Boer (36) found inconsistent results among eight major genotypes: serotonin (5-HTT), dopamine (DRD2, DAT), gluco-corticoid (GR), GABA (GABRB), apolipoprotein systems (APOE2), brain-derived neuro-trophic factor (BDNF) and neuro-peptide Y (NPY). According to Binder et al. (37), several single-nucleotide polymorphisms (SNPs) in FK506 binding protein 5 (FKBP5) interact with childhood trauma to predict severity of adult PTSD. These findings suggest that individuals with these SNPs who are abused as children are more susceptible to PTSD as adults (38).

As can be seen from the above examples, the potential for creative research in this field is huge. However, though it is widely accepted that epigenetic factors can play an important role in the development and transmission of PTSD, “there have been no empirical demonstrations of epigenetic modifications per se in association with PTSD or PTSD risk” (12, p. 430). Uncovering the heritable biomarkers that are involved in TTT would thus be an important task for future research.

Many years of brain research has shown that human beings are “hard-wired” for stress through an intricate pattern of neural pathways designed for the fight-or-flight response. Research also suggests that chronic stress appears to destroy brain tissue, specifically the hippocampus and much of research on the fear response in humans has focused on the activating of the amygdala in subjects with PTSD (39).

Intergenerational effects related to PTSD and HPA-axis stress reactivity are also likely via epigenetic mechanisms (26). New techniques are investigated to search the genome or gene modifications that have been identified as epigenetic risk factors. But while the majority of the initial investigations into main effects of candidate genes hypothesized to be associated with PTSD risk have been negative (40), promising avenues of inquiry into the role of *epigenetic modifications* have been proposed and future studies of PTSD *epigenotypes* may help to elucidate the

neurobiology of inherited PTSD. Epigenomic studies that look at patterns of methylation in many loci and particularly on candidate genes are presently conducted in various places. Similar to the Human Genome Project (41), a new public/private collaboration has initiated a Human Epigenome Project which aims to “identify, catalogue and interpret genome-wide DNA methylation patterns of all human genes in all major tissues” (42). This project is searching for a particular form of a gene variation on a specific chromosome which makes some people more likely to develop PTSD than others. While simplified biological models may not properly capture the complex etiology of PTSD (43), and though studies of genotype may only present a limited picture of the molecular biology of this disorder, there seems to be a clear rationale for examining genetic factors in PTSD in conjunction with environmental factors, such as trauma exposure. The examination of epigenetic mechanisms together with gene expression might help refine models that explain how PTSD-risk and recovery are mediated by the environment (32).

CONCLUSION

Presenting such verifiable data of TTT would have far reaching consequences. First of all, it would continue to reinforce the paradigm shift in scientific thinking that underscores the impact of stressful events on the physiology not only of the trauma survivors themselves, but also of their offspring (23). Furthermore, improved understanding of epigenetic transmission of PTSD in children of trauma survivors would allow a more accurate diagnosis, improved prevention and more targeted treatment interventions of such clients, possibly leading to a sort of “epigenetic medicine” (44). Specific epigenetic therapies could hold promise for a wide range of biological applications, from cancer treatment to the development of induced stem cells (45), as well as for a more targeted treatment of TTT. Finally, any such verifiable data of trauma transmission would have legal consequences for generations of trauma survivors who may want to claim reparation for their epigenetically inflicted wounds.

Most importantly, however, new epigenetic data have the potential to settle some controversies from previous research. Recent overviews of such research (46-49) concluded that the contrasting forces of vulnerability and resilience were both present in Holocaust survivors and their children. But how did the first generation of severely traumatized survivors achieve so much, and how

can their children function so well when bearing such a heavy burden? And how can we explain that offspring who came to psychotherapy complained so much about various kinds of secondary traumatization effects, while epidemiological studies repeatedly failed to show that they were any different from comparable populations? Clinical observations and controlled research were consistently divided in their assessment of this population for many decades. With the added use of epigenetics, however, this dispute becomes much more reconcilable. Epigenetic transmission models make the discrepant findings regarding the presence or absence of specific psychopathology as well as the simultaneous presence of both frailty and hardness in this population much more explicable. Because from the point of view of epigenetics, any inherited (genetic) dispositions can be either turned on or off, and thus activate either overwhelming anxiety or sufficient coping in the same person at different times, according to certain aggravating and mitigating (environmental) factors (3). As emphasized by Yehuda and Bierer (12), “integrating epigenetics into a model that permits prior experience to have a central role in determining individual differences is also consistent with a developmental perspective of PTSD vulnerability” (p. 432).

Finally, epigenetics opens up a potentially more optimistic view of health and disease in offspring of trauma survivors. Since epigenetics conveys that human beings are not only predestined, but also highly malleable creatures, they are able to reverse the deleterious effects of trauma and find some closure to the endless multigenerational saga. This may be achieved either through a variety of established psychotherapeutic interventions or through new psycho-pharmacological drugs, or a combination of both. Even though such offspring might still be more or less influenced by their genes and despite their physiological predestination, they might realize that it's up to them to decide what to do with all of it. Instead of succumbing to the emotional effects of the past tragedies, they might search and find some kind of personal transformation journey that gives new meaning to their legacy.

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