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Biological pathways for historical trauma to affect health: A conceptual model focusing on epigenetic modifications

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ABSTRACT

Despite their unique histories, environments, and lifestyles, historically subjugated populations consistently show poorer health outcomes compared to the general population. The theory of historical trauma, which argues that a collective trauma experienced by one generation can negatively impact the wellbeing of future generations, is a potential framework to understand the adverse health outcomes seen among populations with histories of subjugation. However, the biological pathways through which historical trauma actually impacts health have been unclear. In this paper, we present a cumulative, two pathway model that describes how historical trauma can impact health in contemporary generations. The first pathway suggests that personal exposure to trauma or stressors, which are more common among populations that have experienced historical trauma, can induce epigenetic modifications that can contribute to the development of poor health. The second pathway posits that poor health can occur through intergenerational epigenetic modifications in response to parental and grandparental trauma or stressor exposures. Taken together, these pathways can provide insight into the higher rates of adverse health outcomes among individuals from populations that have historically endured collective trauma. Importantly, the potential reversible nature of epigenetic modifications suggests that these trauma-induced epigenetic effects are not necessarily permanent and that improvements in environmental conditions could reduce the high prevalence of poor health among historically disadvantaged communities.

1. Introduction

Ka mo'opuna i ke alo or “the grandchild in the presence,” is a Hawaiian proverb that describes the importance of being conscious of how one generation impacts future generations. This old adage encompasses the core concept of historical trauma, which is here described as a collectively experienced trauma in an ancestral generation that is associated with poor mental and physical health outcomes in descendent generations (for a list of additional definitions of historical trauma, see [Supplementary Table 1](#); [Brave Heart and DeBruyn, 1998](#); [Denham, 2008](#); [Evans-Campbell, 2008](#); [Hartmann and Gone, 2014](#); [Maxwell, 2014](#); [Mohatt et al., 2014](#); [Sotero, 2006](#); [Walters et al., 2011a](#); [Whitbeck et al., 2004](#)). The intellectual lineage of historical trauma theory can be traced to studies that empirically evaluated the outcomes of the offspring of Holocaust survivors ([Kellermann, 2001](#)). These studies showed that children of Holocaust survivors were likely to have lower self-esteem, suffer from psychological disorders (e.g. post-traumatic stress disorder (PTSD)), and have poorer physical health than their counterparts whose parents were also Jewish, but did not directly experience the Holocaust. Since these initial studies, researchers have

recognized that this theory could be used to describe the development of poor health outcomes in groups that have undergone traumatic exposure to war (e.g. Japanese Americans during internment in World War II ([Nagata et al., 2015](#)) and prisoners of the Yom Kippur War ([Zerach et al., 2017](#))), as well as populations that have been historically and systematically subjugated (e.g. Native Americans ([Brave Heart and DeBruyn, 1998](#)), Mexican Americans ([Estrada, 2009](#)), and African Americans ([Simon et al., 2000](#))).

While the effects of historical trauma on health are evident to members of many historically disadvantaged communities, this concept has not received as much formal attention in public health literature. Part of the reason for this neglect is that the biological mechanisms through which social experiences in one generation could shape biology and health in subsequent generations were unclear. We now know that environmental experiences, including exposure to trauma and stressors, can impact individual and offspring biology through epigenetic modifications ([Gravlee, 2009](#); [McDade et al., 2017](#); [Mulligan et al., 2012](#); [Tehrani et al., 2013](#); [Thayer and Kuzawa, 2011](#); [Thayer and Non, 2015](#); [Weaver et al., 2004](#); [Yehuda et al., 2015, 2014](#)). These epigenetic modifications induce changes in gene expression that can affect the

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regulation of a broad range of physiological systems including the stress, immune, and cardiovascular systems (Bowers and Yehuda, 2016; Mehta et al., 2013; Paccaud et al., 2015; Saban et al., 2014; Thayer and Kuzawa, 2011). Therefore, exposures to trauma and stressors can result in modifications to the epigenome, and these changes can affect biological functioning and chronic disease risk, potentially across generations.

Building on prior theories of historical trauma (Brave Heart and DeBruyn, 1998; Denham, 2008; Evans-Campbell, 2008; Hartmann and Gone, 2014; Maxwell, 2014; Mohatt et al., 2014; Sotero, 2006; Walters et al., 2011a; Whitbeck et al., 2004) and ecosocial and biosocial approaches to understanding health (Harris and McDade, 2018; Hoke and McDade, 2014; Krieger, 2001), we have developed a model of two cumulative pathways whereby historical trauma can influence contemporary health through epigenetic modifications. In the first pathway we argue that exposure to trauma and stressors across the life course, which is more common for populations that have experienced historical trauma (Boutwell et al., 2017; Kaiser Family Foundation, 2017; Kenney and Singh, 2016; Kirmayer et al., 2000), can induce changes to the epigenome that can increase the risk of developing poor health. We then argue in our second pathway that stress-induced epigenetic effects, established in parental generations, can affect the biology and health of descendant generations through intergenerational effects. This model has important implications for understanding the development of health disparities among historically disadvantaged populations, especially those that have endured collective and systematic exposures to trauma. Since epigenetic modifications can potentially be reversed (Waterland and Jirtle, 2003), understanding associations between trauma, stressors, and the epigenome could facilitate the development of interventions that might reverse trauma- and stress-induced impacts on the epigenome, thus reducing the burden of adverse health outcomes within historically marginalized communities.

1.1. Biological mechanisms through which trauma can impact health: a focus on the epigenome

Trauma and stress exposure can impact the health of individuals from historically marginalized groups through changes to the epigenome. In the most general terms, the epigenome refers to chemical factors that do not change the genomic sequence itself, but instead, affect phenotypic outcomes by altering the ways that genes are expressed (Felsenfeld, 2014; Jaenisch and Bird, 2003; Lock, 2013; Thayer and Non, 2015). The epigenome is of particular interest in the context of historical trauma theory because it is shaped by both genetic variation and environmental experiences (Thayer and Kuzawa, 2011). This environmental sensitivity suggests that exposure to trauma or stressors can modify the epigenome which, in turn, can impact gene regulation, expression, and ultimately, patterns of biology and health.

The epigenome includes a broad range of chemical marks such as the incorporation of noncoding RNAs or the modification of histones (Cedar and Bergman, 2009; Felsenfeld, 2014). Currently, the most widely studied form of epigenetic mark is DNA methylation, which is the attachment of a methyl group to a cytosine neighbored by a guanine (termed a CpG dinucleotide; Cedar and Bergman, 2009). Since methylation is sensitive to environmental exposures such as trauma and stressors and can program physiological functioning, environmentally-induced changes in DNA methylation represent a viable biological pathway for trauma and stressor exposure to affect health.

Studies have provided evidence that the timing of epigenetic sensitivity to the environment extends across the life course, including into the prenatal period. For example, one study found that paternal stress was associated with differences in microRNAs in sperm in mice, which in turn, was linked with offspring Hypothalamic Pituitary Adrenal (HPA)-axis dysregulation and altered stress reactivity (Rodgers et al., 2013). Further, Perroud et al. (2014) found that the *NR3C1* (glucocorticoid receptor gene) promoter in children of Tutsi mothers who

were pregnant during the Rwandan genocide had higher rates of hypermethylation compared to Tutsi mothers and children not exposed to the genocide. A meta-analysis found that hypermethylation at this specific gene promoter was also associated with maternal experiences of stress during pregnancy (Palma-Gudiel et al., 2015). Changes in methylation at the *NR3C1* promoter are of particular interest because its expression can impact the function of the HPA-axis, which is one of the primary physiological systems that manages the organismal stress response (Thayer et al., 2018). DNA methylation-induced changes in HPA-axis function can precede the development of chronic conditions, including metabolic syndrome and mental health disorders (Joseph and Golden, 2017; Kuehl et al., 2015). These findings suggest that parental stress can modify the epigenome and stress physiology in both the parent and offspring, and that these changes can impact both mental and physical health outcomes.

Parental programming of offspring epigenome likely occurs through a combination of germline and environmental effects. While most DNA methylation marks are removed twice during development in mammals, first in primordial germ cells, and again following fertilization (Felsenfeld, 2014; Heard and Martienssen, 2014), recent research has shown that methylation at a limited number of loci can be maintained through multiple generations (Boskovic and Rando, 2018). In odor fear conditioning of mice, researchers found induced heritable changes to sperm DNA, and observed behavioral effects two generations later, suggesting the germline inheritance of methylation marks (Dias and Ressler, 2013). In humans, Serpeloni et al. (2017) studied epigenetic effects across multiple generations, and found methylation at five CpG sites that significantly correlated with grandmaternal experience of violence during pregnancy. These studies suggest that while trauma and stress impact the epigenome of those exposed, the effects of exposure can be maintained across at least two generations.

While prenatal exposures have important effects on epigenetic marks, early stages of postnatal life also determine epigenetic profiles in individuals (Weaver et al., 2004). For example, patterns of maternal care have been associated with distinct differences in DNA methylation at the *NR3C1* promoter, stress physiology, and adulthood behavior in rats (Weaver et al., 2004). A post-mortem analysis of human suicide victims found methylation differences at the *NR3C1* promoter between those that experienced childhood abuse and those who did not (McGowan et al., 2009). Importantly, both of these studies assessed methylation of this promoter in the hippocampus, which is where epigenetic modifications to this specific gene are presumed to be functionally relevant in terms of its impact on stress physiology functioning.

Notably, epigenetic modifications resulting from environmental exposures, such as early stress or adversity, are not necessarily permanent (Allis and Jenuwein, 2016). Most famously, the Agouti mouse model demonstrates that nutritional intervention can reverse prenatally established methylation marks, with prominent effects on offspring phenotype (Waterland and Jirtle, 2003). The administration of growth hormone has been found to reverse programming effects of malnutrition in animal models, in part through epigenetic regulation of gene expression. In humans, maternal stroking behavior in the postnatal period can reverse the observed effects of maternal depression on offspring epigenome (C Murgatroyd et al., 2015). The potential reversible nature of epigenetic marks emphasizes the importance of studying epigenetic variation associated with historical trauma experience to identify possible epigenetic targets for intervention. These might be nutritional, behavioral, or pharmacological in scope; however more research is needed to understand how such interventions might work (Murgatroyd and Spengler, 2011). In addition, longitudinal studies assessing epigenetic variation at multiple time points could further enhance our understanding of relative stability or flexibility in these markers in response to environmental exposures.

In sum, there is strong evidence that exposure to trauma and stressors can shape the epigenome and impact biology and health

Biological Pathways for Historical Trauma to Affect Health

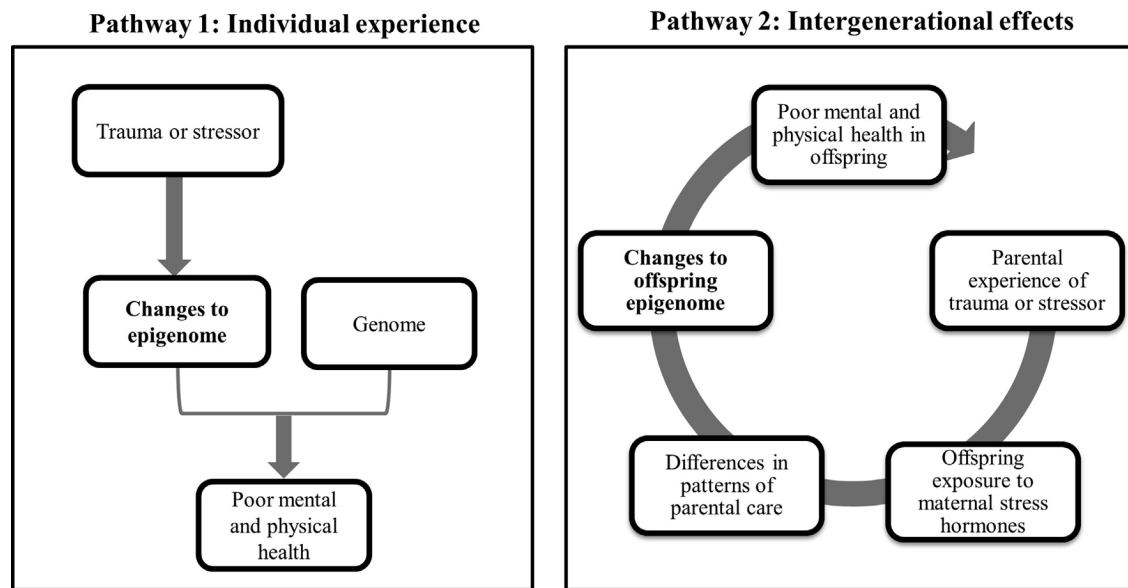


Fig. 1. Conceptual model focusing on how epigenetic modifications can facilitate the relationship between historical trauma and contemporary health. Pathway 1 and 2 are cumulative pathways that explain how historical trauma can contribute to contemporary health disparities through epigenetic modifications. Pathway 1 suggests that exposure to trauma or stressors, which is more common among populations that have experienced historical trauma, can impact the epigenome which, by interaction with the genome, can contribute to poor mental and physical health. Pathway 2 suggests that parental experience of trauma or stressors can impact mental and physical health outcomes in offspring through intergenerational epigenetic effects in both the prenatal and postnatal period.

outcomes, and that these effects may transcend generations. The potential reversibility of these marks suggests that epigenetic changes resulting from trauma or stress are not necessarily permanent and that interventions could potentially reverse trauma- or stress-induced epigenetic modifications.

2. Conceptual model of historical trauma: two pathways

We propose two, cumulative pathways whereby epigenetic modifications can facilitate the relationship between historical trauma experience and the development of poor health in contemporary generations (Fig. 1). In the first pathway, we argue that exposure to trauma or stressors, which is more common among populations that have experienced historical trauma (Boutwell et al., 2017; Kaiser Family Foundation, 2017; Kenney and Singh, 2016; Kirmayer et al., 2000), can contribute to the development of poor health by epigenetic alterations that shape physiological functioning and disease risk. In the second pathway, we argue that epigenetic modifications induced by trauma or stress established in Pathway 1 can be transmitted through intergenerational effects to offspring epigenome, which in turn can shape disease risk in offspring. Our model is described in greater detail below.

3. Pathway 1: high exposure to trauma and stressors among populations that have experienced historical trauma induce epigenetic modifications that contribute to poor health

As briefly described above and further expanded upon below, the impacts of trauma and stressor exposure across the life course on the epigenome and health are becoming increasingly well understood (Kuzawa and Sweet, 2009; McGowan et al., 2009; Mehta et al., 2013; Saban et al., 2014; Swartz et al., 2016; Tehranifar et al., 2013; Thayer and Kuzawa, 2011; Walters et al., 2011b). Importantly, populations that have experienced historical trauma are more likely than historically advantaged populations to be exposed to trauma and stressors known to induce epigenetic modifications (Boutwell et al., 2017; Kaiser

Family Foundation, 2017; Kenney and Singh, 2016; Kirmayer et al., 2000). For example, Indigenous children experience disproportionately higher rates of adverse childhood experiences (ACEs), including abuse and neglect (Kenney and Singh, 2016; Kirmayer et al., 2000). Kenney and Singh (2016) showed that while American Indian and Alaskan Native (AI/AN) children are at a higher risk for exposures to ACEs, they are also more likely to accumulate multiple ACEs over time. Research has also shown that in the United States 61% of African American children experience ACEs, compared to 41% of non-Hispanic white children (Sacks and Murphey, 2018). AI/AN and African Americans are also twice as likely to be living in poverty than the general population, thus increasing risk of exposure to financial insecurity and other associated stressors (Kaiser Family Foundation, 2017).

In addition to being more frequently exposed to trauma and stressors in general, as Mohatt et al. (2014) and Sotero (2006) discuss, there are particular types of stressors that may be uniquely experienced by populations that have endured historical trauma. These unique stressors might include a Navajo woman in the present day who cannot speak her tribe's indigenous language and is therefore unable to communicate with her elders. Her lack of cultural knowledge can be traced to earlier government policies of assimilation in an ancestral generation that made speaking the native language illegal (Whitbeck et al., 2004). Contemporary stressors may also take the form of public reminders of historical subjugation (Mohatt et al., 2014). For example, Native Americans may be reminded of the historical trauma of colonization upon the erection of commemorative statues of controversial American icons such as George Custer, famous for his 'last stand' of the American Indian Wars that decimated Indigenous populations across the West (Elliott, 2007). Confederate statues across the United States have recently been removed as people recognized the divisive message the public commemoration of these individuals sends (Savage, 2018).

Pathway 1 (Fig. 1) argues that exposure to trauma or stressors, experienced more frequently by populations that have faced historical trauma, can lead to poor mental and physical health through epigenetic mechanisms. Specifically, epigenetic modifications induced by trauma

and stressor exposures interact with the genome to affect gene expression and resulting biology, such as the stress response system (Houteven et al., 2016; Kertes et al., 2016; Non et al., 2016), which can then influence the development of adverse health outcomes.

Below we discuss evidence that trauma and stress exposure can shape the epigenome and health. We focus on three types of stressors that are more common to populations that have experienced historical trauma and discuss associated health impacts and, where evaluated, epigenetic modifications: low socioeconomic status, discrimination, and historical loss.

3.1. Low socioeconomic status

Within the United States, individuals with the lowest incomes have consistently poorer physical and mental health outcomes (Braveman et al., 2010). This finding has been replicated in many populations internationally, including countries with universal access to health care (Canadian Institute for Health Information, 2015; Fujita et al., 2016). These associations are often continuous across the income spectrum, suggesting that they reflect more than just material deprivation and that perceived inequality may significantly contribute to this relationship (Fuller-Rowell et al., 2012; Goodman et al., 2007; Sapolsky, 2005). Importantly, populations that have experienced historical trauma are more likely to experience poverty and low income in the present day (Kaiser Family Foundation, 2017).

Low socioeconomic status (SES) has been associated with alterations in epigenetic methylation (Paccaud et al., 2015; Tehranifar et al., 2013). For example, Paccaud et al. (2015) found that low SES was predictive of hypomethylation at genes involved in immune responses. Uddin et al. (2013) looked at the role of SES in a trauma-exposed cohort and found that individuals with low SES had altered methylation patterns at genes responsible for regulating the nervous system response in stress reactivity. Further, in a study on SES and mental health outcomes, Swartz et al. (2016) found an increase in methylation at the proximal promoter of the serotonin transporter gene in adolescents who were of low SES. This increased methylation, in turn, was associated with greater threat-related amygdala reactivity (Swartz et al., 2016).

3.2. Discrimination

Sotero (2006) explains that while overt forms of subjugation may be dismantled over time, the legacy of subjugation remains in the form of discrimination. Therefore, while discrimination may be experienced by individuals from populations without historical trauma, discrimination is particularly impactful for descendants of populations affected by historical trauma because discrimination incidents are often rooted in the subjugation and mistreatment of their ancestors. Discrimination has been shown to correlate with poor health outcomes for historically subjugated populations (Pascoe and Smart Richman, 2009; Pieterse et al., 2012). Specifically, studies have shown that increased levels of perceived discrimination are linked to higher levels of stress hormones (Thayer and Kuzawa, 2011), blood pressure (Dolezsar et al., 2014; Thayer, 2017), obesity (Cozier et al., 2014; Hunte and Williams, 2009), and overall mortality (Barnes et al., 2008).

Experiences with discrimination have been associated with epigenetic patterns that likely influence these poor health outcomes (Brody et al., 2016; Chae et al., 2014; Kuzawa and Sweet, 2009). Kuzawa and Sweet (2009) argue that disparities in cardiovascular health outcomes between African American adults and white adults in the United States may relate to historical and contemporary experiences of discrimination, and that these impacts may be facilitated by changes to the epigenome. Consistent with this argument, Brody et al. (2016) found that African American children who were exposed to higher levels of discrimination and lacked a supportive environment had greater epigenetic aging, an indicator of non-mitotic cellular aging. Discrimination has also been associated with shorter telomere length, a mark of mitotic

cellular aging, among African American men (Chae et al., 2014).

3.3. Historical loss

Historical loss represents feelings of loss directly resulting from the experience of historical trauma and have been associated with health disparities in Indigenous populations. Two scales have been developed to measure this: 1) the Historical Loss Scale and 2) the Historical Loss Associated Symptoms Scale (Whitbeck et al., 2004). Both specifically detect present-day perceptions and feelings of loss of cultural and material items resulting from colonization (Whitbeck et al., 2004). These measurements, developed by Whitbeck et al. (2004), focus on twelve types of losses, including the loss of land, language, traditions, values, family ties, trust, and respect, which are all consequences of subjugation and assimilation.

In a study that utilized these assessments with Native American children from the Upper Midwest region, adolescents were found to be highly cognizant of the consequences of historical trauma experienced by their ancestors (Whitbeck et al., 2009). One-fifth of the children in this study reported thinking about historical losses on a daily basis, and in some cases, children thought about losses more often than adults, indicating that effects of historical trauma remain relevant to children in the present-day (Whitbeck et al., 2009).

Armenta et al. (2016) gathered data using these scales and found that adolescents who thought more about historical loss had higher levels of anxiety, providing support for the concept that historical loss can be psychologically distressing for adolescents even if they were not in the generation directly exposed to the historical trauma. A study on Native American college students in the Southwest found that those who experienced historical loss had higher levels of depression and anxiety and lower levels of resilience (Altaha and Kraus, 2017). Among American Indian adults in the Midwest, it was also found that notions of historical loss remained relevant into late adulthood and was correlated with feelings of anxiety and depression (Whitbeck et al., 2009). These studies show that impacts of historical trauma are sustained through subsequent generations, and that such impacts are associated with poorer mental and physical health outcomes. Future studies should investigate whether historical loss is associated with variation in epigenetic modifications, particularly at genes relevant to the mental health outcomes described above.

Measures of loss and discrimination have also been assessed simultaneously. Pokhrel and Herzog (2014) assessed both historical loss and discrimination experience in a Native Hawaiian cohort of college students and concluded that historical trauma prevalence measured through loss could increase substance abuse via greater perceived discrimination.

3.4. Summary

Trauma and stressors can lead to poor health, in part, through modifications to the epigenome. These epigenetic changes are important in that they interact with the genome to affect gene expression, which ultimately result in phenotype establishment in biological systems. Since trauma and stressors are more frequently experienced among populations that have experienced historical trauma, this suggests that these populations may experience a greater burden of poor health as a result. Importantly, some of the stressors experienced by populations that have experienced historical trauma, such as historical loss, may be uniquely experienced by these communities.

4. Pathway 2: poor health outcomes in descendent generations can accrue through intergenerational epigenetic effects

Our second pathway (Fig. 1) suggests that historical trauma can shape contemporary health because environmentally-induced epigenetic modifications in parents can influence offspring biology and

health. This part of our model builds directly on the developmental origins of the health and disease (DOHaD) hypothesis, which argues that prenatal and early life exposures can shape health in later life (Kuzawa and Quinn, 2009). In particular, maternal experiences of nutritional and psychological stress in pregnancy, as well as parental experience of stress and depression in the postnatal period, are associated with an increased risk of adverse physical and mental health conditions for offspring in adulthood (Thayer and Kuzawa, 2011). Pathway 2 therefore recognizes that the biological and behavioral outcomes resulting from parental exposure to trauma and stressors can have intergenerational effects on offspring epigenome and health.

Below we consider three ways in which parental experience of trauma and stressor exposure can lead to poor offspring health via epigenetic modifications: intrauterine signaling, breast milk composition and breastfeeding behavior, and patterns of parental care.

4.1. Intrauterine signaling

In development, a period of large epigenetic malleability coincides with a period of transfer of hormones and other information between mother and child (Kuzawa and Quinn, 2009). Due to this overlap, aspects of the intrauterine environment, including hormone and nutrient composition, can shape offspring epigenome. Relevant to historical trauma, a large number of studies have assessed the relationship between maternal stress during pregnancy and epigenetic methylation of the *NR3C1* promoter (Mulligan et al., 2012; Oberlander et al., 2008; Yehuda et al., 2014). Mulligan et al. (2012) found an association between war trauma exposure during pregnancy for women from the Democratic Republic of Congo with methylation variations at the *NR3C1* promoter gene, and that variation in turn was correlated with lower offspring birth weight. Cao-Lei et al. (2015) studied the offspring of women who were pregnant during the 1998 Quebec ice storm and found that prenatal maternal stress associated with this storm was associated with alterations in DNA methylation in several tissues in offspring at 13.5 years of age. These changes in methylation were correlated with physiological outcome measurements of greater central adiposity and body mass index.

In the prenatal period there have also been many studies focused on methylation changes as a result of maternal mood and stress during pregnancy. For example, Oberlander et al. (2008) found that prenatal maternal depression was associated with neonatal methylation of the *NR3C1* glucocorticoid receptor gene promoter and greater infant HPA-axis reactivity. Increased offspring methylation at this promoter has also been associated with maternal anxiety (Hompeš et al., 2013). These studies show that through intrauterine signaling, the experience of negative maternal mood or stress during pregnancy can manifest in alterations in epigenetic patterns of offspring, with potential long-term effects on health outcomes.

4.2. Breastfeeding behavior and breast milk composition

A lack of breastfeeding can have important effects on offspring health. A shorter duration of exclusive breastfeeding is more common among women experiencing stress, socioeconomic marginalization (Temple Newhook et al., 2017), and food insecurity (Orr et al., 2018). In addition, maternal stress, poverty, and minority status, all of which are more common among populations that have experienced historical trauma, predict reduced initiation and duration of breastfeeding. For offspring, shorter breastfeeding is associated with increased infectious disease, childhood obesity, type 1 and type 2 diabetes, and sudden infant death syndrome (Bachrach et al., 2003; Horta and Victora, 2013a, 2013b; Stuebe, 2009; Victora, 2000).

Breast milk composition, which can vary with respect to nutrients, hormone levels, microbiome, and immune factors, can also contribute to variation in offspring developmental and health outcomes (Bosquet Enlow et al., 2017; Hahn-Holbrook et al., 2016; Hinde et al., 2015).

Hinde et al. (2015) looked at cortisol in the milk of rhesus macaques in relation to infant temperament and found that increased glucocorticoid levels predicted the establishment of a less confident, nervous temperament. Human studies have also shown that higher concentrations of cortisol in breast milk is predictive of infant induced fear reactivity (Nolvi et al., 2017), negative affectivity (Bosquet Enlow et al., 2017), temperament (Jonas et al., 2015), as well as BMI (Hahn-Holbrook et al., 2016). While methylation changes in response to cortisol in breast milk has not been assessed directly, it is possible that epigenetic changes mediate these effects (Verduci et al., 2014).

4.3. Parental care

Patterns of parental care are also important for shaping offspring epigenome and health outcomes in the postnatal period. Mirroring the Weaver et al. (2004) study of maternal contact in mice, C. Murgatroyd et al. (2015) provided evidence for a similar dynamic impact of early life stress on DNA methylation in humans. The study found increased methylation of the *NR3C1* promoter in infants who had mothers that experienced low prenatal depression followed by high postnatal depression. Interestingly, the effect was reversed by self-reported maternal stroking over the first weeks of the infants' lives, providing evidence for the plasticity of epigenomic programming in early life.

Adverse childhood experiences (ACEs), like abuse, which are experienced more frequently by populations that have experienced historical trauma (Kenney and Singh, 2016; Sacks and Murphey, 2018) have also been associated with increased methylation at the glucocorticoid receptor gene (Perroud et al., 2011; Tyrka et al., 2016) and with microRNAs in sperm (Dickson et al., 2018). Houtepen et al. (2016) found a correlation between childhood trauma, genome-wide DNA methylation, and overactive stress reactivity. Additionally, Non et al. (2016) found different methylation patterns in two stress related genes (*FKBP5* and *SLC6A4*) that were associated with early life institutionalization in Romanian orphanages. These findings of increased methylation in relation to ACEs are important because ACEs are also linked to poor outcomes in adulthood. In a study of American Indians in South Dakota, Warne et al. (2017) found that ACEs were associated with increased alcohol use and smoking in adulthood. In another study, Thayer et al. (2017) studied Northern Plains American Indians and reported a link between ACEs, higher PTSD, and allostatic load in adulthood. Thus, patterns of parental care and associated experience of ACEs can initiate epigenetic changes that can affect the physiological and psychological health of the child, even in adulthood.

4.4. Summary

The intergenerational transmission in Pathway 2 shows how the biological consequences of historical trauma can be inherited across generations through intrauterine environments, changes in breast milk composition and breastfeeding behavior, and patterns of parental care.

5. Applying the model: an example of historical trauma and Native Hawaiian health

Native Hawaiians are a population that has experienced historical trauma, and like many other historically subjugated groups, face health disparities in the present day (Office of Hawaiian Affairs, 2017). We argue that our model can provide an effective conceptual framework for understanding how Native Hawaiian experiences of historical trauma, in this example, the Great Māhele of 1848, can contribute to the high burden of adverse health outcomes within this population. For context, King Kamehameha III initiated the Great Māhele legislation under the direction of American advisors and in response to continued demands of foreigners claiming their “right to own land” (Blaisdell, 2005). The Māhele was the privatization and redistribution of land that operated under the Western notion of land ownership which was antithetical to

the relationship Native Hawaiians shared with their *‘āina* (land) (Wise, 2012). Land ownership was a foreign concept to Native Hawaiians as they did not believe land should be possessed by a single person or business. Instead, Native Hawaiians held a sacred, symbiotic relationship with land in which they considered land similarly as one might consider a relative or ancestor (Wise, 2012). Native Hawaiians who had lived on their land for centuries lacked the Western knowledge, experience, and money that were required to claim their property (Chinen, 1958). As a result, many Hawaiians lost their land, which was then purchased by foreigners after the passage of the Resident Alien Act of 1850 (Chinen, 1958; Wise, 2012).

With the Great Māhele as an example of historical trauma, we can imagine a Native Hawaiian woman during this time who experienced the trauma of a disruption to her cultural beliefs (specifically her relationship with land) and a physical displacement from the land that she lived on and cared for. Using Pathway 1, we argue that the emotional trauma and stress of these experiences could produce environmentally-induced epigenetic modifications at genes related to her stress physiology. These changes to her epigenome would then interact with her genome to affect gene expression regulating her stress response and biology that could ultimately heighten her risk of developing poor mental and physical health.

The daughter of this woman would not have the first-hand experience of losing her land in the Great Māhele but might suffer her own set of trauma and stressors such as the hardships of poverty related to the physical displacement endured by her mother. This daughter's child, two generations removed from the ancestral generation that experienced the Great Māhele, might then no longer be able to live in Hawai'i without facing the threat of homelessness, and experience feelings of the personal loss of her cultural traditions when she is forced to move. The poverty (economic destruction (Sotero, 2006)) experienced by the daughter and the feelings of historical loss (cultural dispossession (Sotero, 2006)) of the granddaughter are both stressors capable of directly affecting these individuals (Whitbeck et al., 2004). Through this example of Pathway 1 of our model, we see that while stressors experienced by contemporary generations do not necessarily occur in the same form as the initial historical trauma event, they are nonetheless important and salient because they can be perceived as being rooted in the subjugation of ones' ancestors. As these stressors continue to disproportionately affect historically marginalized populations, environmentally-induced epigenetic modifications can thereby facilitate the relationship between historical trauma and the development of poor health in these communities.

Using Pathway 2, we can describe how epigenetic modifications in the Native Hawaiian woman directly exposed to the trauma of the Great Māhele can be maintained in, and impact the biology of her child and other future generations. As described above through the mechanisms of Pathway 1, this woman could have developed trauma-induced epigenetic changes that altered her stress physiology. Importantly, this could result in her offspring experiencing a higher exposure to cortisol *in utero* or through breast milk. Further, because of the push towards Western forms of thinking during the Great Māhele, the Native Hawaiian woman might experience emotional distress, which could impact her parenting behavior and subsequently, her offspring's epigenome and health outcomes. Thus, the child and other descendants of the woman who experienced the historical trauma of the Great Māhele might also develop altered methylation at genes associated with stress physiology and experience further associated health complications adults. In this way, health disparities can be maintained in populations that have been historically subjugated by intergenerational epigenetic effects.

In sum, historical trauma results in a greater frequency of trauma and stressor experience for the affected population, and these exposures can directly impact the epigenome and resulting health of the individuals within these communities. In addition, parental experience of trauma can have intergenerational health effects through prenatal and

postnatal effects. Using this model, we can examine the way that historical trauma experiences can contribute to the development of poor health outcomes in contemporary generations through epigenetic modifications.

6. Discussion and future directions

While the potential importance of epigenetic modifications to the theory of historical trauma has been recognized (Walters et al., 2011a), our model has sought to describe the within- and between-generation pathways whereby historical trauma can affect health. We hope that this model encourages empirical studies that evaluate the health impacts of historical trauma, especially in regards to populations that have a history of subjugation and demonstrate a high prevalence of chronic health conditions. If epigenetic modifications are found to facilitate the adverse effects of historical trauma on health outcomes, it is possible that interventions can be designed to reverse these effects.

While we believe that this model has many strengths, there are limitations that need to be addressed in future work. First, we must be cognizant of the dangers of contemporary meaning-making for past traumatic events. As researchers evaluating experiences of ancestral generations in the context of health reparations in the present-day, we must be careful when making assumptions of the traumatic nature of past events (Gone, 2013).

Second, many of the traumas and stressors described here, while common in populations that have experienced a historically traumatic event, are not unique to these populations. For example, other individuals from non-historically disadvantaged populations can experience low SES or discrimination. Therefore any individual that has been exposed to similar trauma or stressors has the potential to similarly develop adverse health outcomes. However, we argue that these stress exposures are particularly salient for individuals from communities who have experienced collective historical trauma, such as colonization and slavery, because the contemporary stressors in these cases can often be traced to an instance of overt, intentional historical subjugation. In addition, exposure to many of these stressors are more frequent among communities that have experienced historical trauma (Baranowsky et al., 1998; Manson et al., 2005; Robin et al., 1997; Williams et al., 2007). This combination of increased salience and higher rates of exposure means that these exposures likely have disproportionately large impacts on health within populations that have experienced historical trauma.

Further, it is important to acknowledge that not all individuals who are exposed to trauma and stressors develop adverse outcomes (McEwen, 2016). As such, there is an important need for studies to incorporate and understand the factors that may buffer the development of adverse outcomes in response to trauma or stressor exposure. Such strength-based approaches are important now only for the development of interventions, but can also reduce stigma and be a positive mechanism for knowledge translation among populations that have historically been described with a deficit-based model (Cooper and Driedger, 2018; Fogarty et al., 2018). In conducting such studies, however, we must be mindful to make sure that the results of this work are not used to place responsibility on individuals to be resilient and instead continue to ensure that attention be paid to broader societal factors that shape patterns of trauma and stressor exposure in the first place. In other words, resilience models must, “emphasize positive influences without discounting risks and vulnerabilities” (Masten, 2011).

Building on this latter point, while this article and model focus specifically on how trauma and stressors can directly shape the epigenome and health, it is important to acknowledge that all of these exposures take place within a broader social, cultural, and political context that also impacts patterns of biology and health (Gravlee, 2009; Krieger, 2012). We view this broader environmental context as strongly correlated to historical trauma, as the nature of colonization or slavery is such that contemporary socioeconomic status is shaped by these

experiences. Therefore, more work should be done to solidify our understanding of the relationships of these related exposures to the historical trauma framework.

While we have primarily focused on studies that assess epigenetic marks in response to contemporary traumas and intergenerational effects, we believe that it would be beneficial to incorporate biomarkers of stress and health (e.g. blood pressure, heart rate variability, and cortisol) that are hypothesized to be associated with epigenomic changes in future work. This is particularly important since, in many ways, the discipline of social and behavioral epigenomics described in this paper is limited relative to studies of intergenerational impacts on physiological systems (e.g. stress physiology and immune function). As an example of the type of work we are suggesting, the Cao-Lei et al. (2015) study cited earlier correlated the trauma of maternal stress DNA methylation, body mass index, and immune function. Studying biomarkers in conjunction with epigenetic modifications is a necessary next step for arguing that any epigenetic modifications associated with the pathways described above contribute to health disparities seen today. Multi-disciplinary research teams would be effective in addressing this type of research in terms of developing studies that could evaluate the Historical Loss Scale, in combination with biomarkers and/or epigenetic markers, across multiple generations.

In sum, we believe that our model of biological pathways for historical trauma to affect health should be viewed as a valid conceptualization for better understanding the health disparities consistently observed among non-related populations that share histories of social subjugation and disadvantage.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.socscimed.2019.04.001>.

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