

SOME RIDERS AND CAVEATS FROM HARD EVIDENCE-BASED CLINICIANS

I always like to give air to opposite views and it must be acknowledged that this field is very much in its infancy. Often the language is confusing, and labels are not used consistently. Even the word transmission is debated, and the field of cultural evolution is fraught with controversies. Some researchers are not convinced by the significance of intergenerational trauma. The argument they advance is that the causal chain of events between causes and effects is poorly demonstrated: there are some minor cases, but they argue that the phenomenon is less significant than we suggest.

Needless, to say, I disagree with this. There is very good evidence in laboratory models for the phenomenon. We don't have the tools to show the exact causal relationships, but this is the case with all complex traits, so I don't know why this one is singled out as requiring extra proof. The same criticism can apply to any psychiatric disease. The conclusions are correlated and inferential. They are not shown by deductive proof. Nothing in science usually is.

THE IMPLICATIONS OF INTERGENERATIONAL TRAUMA

My impression is that intergenerational trauma is even more significant than researchers ever realized. And the implications are mind-boggling. Slavery, forced removals, genocide, sexual violence, colonization.... These all have consequences, some of which last for generations.

I am sometimes asked, if I could make one intervention to increase the health and social problems of South Africans what would it be? Well, there are so many ways to intervene but for me, I would say: "A social worker for every street".



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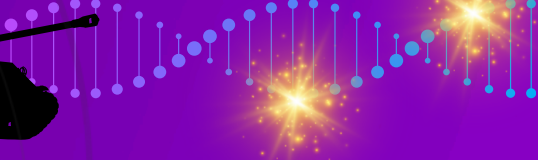
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THINKING ABOUT EPIGENETICS AND INTERGENERATIONAL TRAUMA

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Trauma, whether, emotional, physical, or sexual seems to be everywhere at the moment. I was recently asked about the associated molecular pathology aspects of this issue for a forthcoming book on intergenerational trauma in Gaza. I knew about the phenomenon, but my research impressed upon me just how damaging it is and I share this with you in this newsletter.

WHAT IS INTERGENERATIONAL TRAUMA?

Intergenerational trauma is also called transgenerational trauma. At its core lies the discovery that trauma (and we usually talking about emotional or psychological trauma, but it includes others) experienced by an individual (or group) can be transmitted to successive generations. The stunning part is that the physiological and mental stress is transmitted even when subsequent generations have no direct experience of the trauma. Subsequent generations (and it's not clear for how long this can continue) can have very significant signs and symptoms leading to compromised health, sometimes with catastrophic outcomes. We are talking here about compromised life skills, emotional numbness, personality disorders, depression and anxiety, PTSD, ADHD, and many others etc.

Imagine a refugee, let's call her Amida, from a war-torn area and the physical, sexual and emotional violence that all that entails. Amida finds refuge in a 'safe' country, marries a healthy partner and the couple have a well-rounded, and to all intents and purposes, happy life. Amida falls pregnant with a boy, Dineo. He seems healthy and initially performs well educationally, but in his teenage years begins suffering from major depressive episodes. It's more than teenage-associated challenges, and the family histories (other than Amida's psychological trauma) are non-contributory. Where did Dineo's condition come from?

Answering this question in a definite way that satisfies hardcore empiricists is going to be difficult (we simply don't have the molecular-level tools to do that) but a wealth of evidence suggests the likeliest answer is that Amida's physiological response to trauma was inherited by Dineo. How can this be? How can the trauma be inherited in a genetic or even cultural way? Of course, Amida may share her traumatic history with Dineo, and probably should, but it seems that this on its own is unlikely to have such a dramatic effect.

THE PERSISTENCE OF TRAUMA RESPONSES WITHIN INDIVIDUALS

In hindsight, it shouldn't come as a surprise to learn that even after the trauma or threat has passed, the body and mind do not return to the un-stressed state. We knew this already in cases of PTSD, but it extends to all sorts of traumas. Some of the changes remain for the rest of that individual's life and in very concrete ways. For example, the resetting of resting state levels of hormones like glucocorticoids, or even a resetting of entire endocrine systems like the hypothalamic-pituitary-adrenal axis, is well established. As general practitioners, consider instances where individuals develop hypertension, tremors, and other organic diseases following emotionally stressful periods. The physiological problem can remain for the rest of their lives. As an aside, and a pet peeve of mine, is the Oprah-style pop-psychology argument that one gets closure of these traumas after therapy. That's nonsense, 'closure' is a silly construct. Trauma is not something you deal with in the sense that you 'get over it and move on'. Of course, there are ways of trying to deal with it, to mitigate the impact so that it doesn't remain overwhelming, but you can't un-experience what you experienced. It remains with you in all sorts of ways

THE EVIDENCE FOR INTERGENERATIONAL TRAUMA

There have been numerous studies, and many more are ongoing, that suggest there are several possible mechanisms. Studies come from individuals and populations who escape war zones or genocidal efforts and there are many examples. I will consider one of these.

Afghans have suffered from decades of conflict, displacement, poverty, and efforts to eradicate groups based purely on ethnicity. According to a 2018 EU survey, 85% of Afghans had witnessed at least one traumatic event; 70% require mental health support and 50% suffer from psychological distress to the extent that one-fifth of the population cannot perform routine tasks. Landmark studies revealed how this continues to impact children, grandchildren, and beyond by increasing susceptibility to physical and mental health problems. And almost to the same prevalence as in preceding generations even when there is no direct experience of traumatic events.

Once an individual is removed from the trauma, how can the physiological stress be passed to subsequent generations who don't have first, second, or even third-hand experience of it?

MECHANISMS OF INTERGENERATIONAL TRAUMA

It is difficult to pin down the mechanisms by which the physiological outcomes of trauma pass to offspring, but sound inferences can be made. In laboratory model systems, the mechanisms are more clearly dissected. Of course, one can't do the same experiments on humans (at least from an ethical perspective, although some regimes have tried).

As medical practitioners, we are more inclined to consider the molecular mechanisms, but it is important, probably more so, to emphasize the cultural/psychosocial mechanisms. Cultural transmission of traits (cultural evolution) has become an area of great interest to researchers because the traits can be hardwired and difficult to manage. A simple example is the case of starvation. Obesity is a battle in the offspring of parents who are starved. There is of course a physiological component, but the psychological reference frame for starved individuals is to overeat because it is not known when the next meal may arrive. And the habit is passed on even when food is abundant. And there is also the case that food (often unhealthy ones) causes a change in brain chemistry in a way that ameliorates anxiety and depression associated with periods of starvation. Substance abuse is also both genetically and culturally transmitted.

In the early days of studies of intergenerational trauma, the lack of biological mechanisms meant that explanations were almost exclusively cultural/psychosocial in nature. It was thought that children became vehicles for parental reenactments of fear, grief, rage, etc. However the main mechanism of interest to biologists is epigenetic inheritance (sometimes referred to as one of the kinds of non-genetic mechanisms). There are others like developmental bias, phenotypic plasticity, imprinting, etc., but the details are a lot more sketchy.

EPIGENETIC INHERITANCE OF TRAUMA RESPONSES

Without going into too much detail, epigenetic mechanisms are how genomes are modified by chemical tags that regulate gene expression. The genome sequence is not altered but its expression is. Two broad kinds of epigenetic inheritance are known. First, there are the so-called 'developmentally programmed' effects. These result from the influence of the offspring's early environmental exposures; this can be in utero or the early years of life. The younger an individual is, the more likely they are to have epigenetic stress responses and pass these on to their own offspring. Second, there are the more surprising mechanisms of epigenetic changes associated with preconception trauma. The epigenetic changes are recorded in germ cells and can be sex-specific. These explain the different effects of maternal and paternal trauma, as well as the different manifestations of inherited trauma responses in boys and girls. Children respond differently to family histories of violence depending on multiple factors: the gender of the parent, the stage of life when the parent experienced the trauma, the gender of the child, etc.

As indicated earlier, the hypothalamic-pituitary-adrenal axis is often implicated, but there are others as well. Sympathetic overactivation is reported and then there are unexplained differences found in intracranial volume and grey matter.

NON-EPIGENETIC INHERITANCE

The studies of paternal transmission of trauma responses have been particularly helpful because they control for fetoplacental and other gestational effects. These investigations have revealed that transmission is not only via epigenetic modifications to DNA and histones. Regulatory RNAs play a significant role. These include small noncoding RNA, microRNA and interfering RNA. The mechanisms in these cases are enormously complex and are only now being studied in detail.