Effects of Childhood Trauma and Maltreatment on Gene Expression

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INTRODUCTION

Epigenetics is long term DNA modification that does not affect the sequence but does control gene regulation and expression (Ramo et al.). DNA methylation is the addition of a methyl group to a CpG site. Research shows that the environment can affect DNA modification and gene expression (Ramo et al.). There is evidence supporting increased risk of conditions such as depression or post traumatic stress disorder (PTSD) in adulthood due to childhood trauma. Two genes that react with early trauma to cause increased response to stress situations are the FKBP5 and NR3C1 genes (Klengel et al.).

OBJECTIVES

Our research of literature investigates how childhood trauma and maltreatment affects genes and the lifelong permanent implications of it. This research is also aimed to bring public awareness to the effects of childhood maltreatment.

METHODS

- Literary Search using Academic Search Complete and Google Scholar.
- Key words: epigenetics, childhood trauma and maltreatment, gene expression.

RESULTS

FKBP5 Gene

- FKBP5 is an important regulator of the glucocorticoid receptor complex and is vital in the stress hormone system in ending the stress response at the end of a threat through negative feedback (Klengal et al.).
- Stress and trauma activate the glucocorticoid receptor and induce FKBP5 transcription (Klengal et al.).
- Methylation is important in this cycle to reduce expression of the gene and turn off stress responses.

Research at Max Planck Institute of Psychiatry

- It was found that repeated trauma and stress signals in childhood led to reduced methylation of FKBP5 and resulted in increased cortisol release due to a hyper expression of the gene (Ramo et al.). This led to a prolonged stress response (Ramo et al.).
- Childhood trauma left permanent epigenetic marks on the DNA and repressed FKBP5 transcription, and ultimately led to psychiatric illnesses. Klengel examined the DNA of 2000 Afro-Americans who had been repeatedly traumatized as children and discovered that ⅓ now had PTSD. No disease-related demethylation was detected in those traumatized in adulthood (BM/HR).

NR3C1 gene

- The NR3C1 gene codes for glucocorticoid receptors where hormones dock (Barclay).
- Studies of mother-infant interactions found that children who experienced lower maternal care had hyper-methylated NR3C1 genes leading to lower expression of the gene and higher stress reactivity (Ramo et al.).
- Children reported with maltreatment were also discovered with these epigenetic changes. Consequently they had fewer glucocorticoid receptors and were less able to handle stress leading to health issues later in life (Barclay).

Future implications

- The lasting effects due to these genes include an increased risk of developing stress-associated disorders in adulthood (Klengal et al.). These include PTSD, bipolar disorder, anxiety and depression (Ramo et al.).
- Studies have shown risks for other health issues such as heart disease, obesity, and diabetes (Ramo et al.).
- Individuals can be more prone to infection and cancer (Ramo et al.).

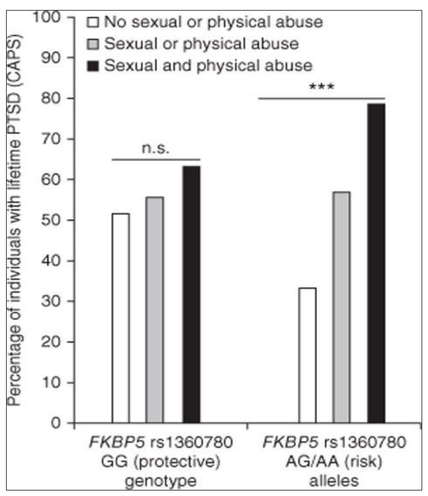

Figure 1. Shown is the interaction of child abuse and *FKBP5* rs1360780 protective genotype (left) or risk allele carrier status (right) on percentage lifetime PTSD.

CONCLUSIONS

Child abuse interactions with the FKBP5 gene enhance its responsiveness. This results in higher risk for trauma-associated psychiatric, immune and metabolic disorders once adults. This can also predispose these children to both PTSD and depression. Demethylation of the FKBP5 gene and hyper-methylation of the NR3C1 gene are shown to significantly predict children's depression and adult PTSD.

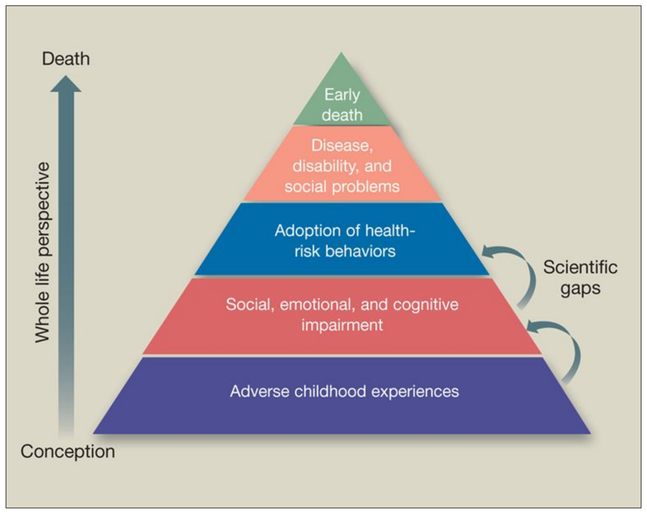

Figure 2. Adverse childhood experiences pyramid showing how long-term effects of early childhood trauma may eventually leads to poor health outcomes in adulthood (Hinch et al.).

FUTURE WORK

Future studies are needed to understand the impact of epigenetic changes transgenerationally. Some studies show that these modifications are heritable but they are not conclusive.

Also further research is needed to understand how epigenetics affect cardiovascular disease, diabetes, and obesity.

There are still no known treatment options that target these CpG sites and reduce the likelihood of psychiatric disorders due to trauma.

References

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