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A MATHEMATICAL MODEL PREDICTS HPA AXIS RESPONSE IN LATE ADULTHOOD DUE TO CHILDHOOD SEPARATION

S. Lakshmi* and S. Alamelu**

* Associate Professor of Mathematics, K.N.Govt.Arts College for Women, Thanjavur.(T.N.)

Email: lakshmi291082@yahoo.co.in

**Assistant Professor of Mathematics, S.D.N.B.Vaishnav College for Women, Chennai (T.N.) , Email: alambalaji@yahoo.com

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ABSTRACT

The aim of this study is to find whether parental separation is associated with salivary and plasma cortisol or plasma ACTH reactivity by mixed model analysis method (i.e.) to analyze differences in the baseline or incremental area under the cortisol or ACTH curves. Analyses using the mixed model show that participants who were separated from both parents had higher salivary cortisol and plasma ACTH concentrations across all time points during the stress.

Weibull Model and Wayne-Nelson's method shows that there is an association between Early Life Stress and HPA axis responsiveness and this stress shows higher reactivity in late adulthood due to childhood separation from both parents and the level of percentage of stress is higher for men than the women and the effect of stress reaches the peak level for the children who are separated between 2 and 7 years of age.

Keywords: Weibull's model , Wayne-Nelson's method, ELS-Early Life Stress

AMS Subject Classification: 60E

INTRODUCTION

A number of studies have been undertaken to determine life distribution functions representing the evolution of stress phenomena in time. Chapouille and deo Pazzis (1968) among others have demonstrated that the study of failure distributions is very well represented by Weibull's distributions. This mathematical model has the advantage of covering a relatively large number of lifetime distributions.

The cumulative distribution function is expressed as follows:

$$F(t) = 1 - \exp\left(-\left[\frac{t-\gamma}{\eta} \right]^{\beta} \right)$$

Where β = shape parameter or Weibull slope
γ = location parameter
η = scale parameter or characteristic life

Probability density function f(t) is given by:

$$f(t) = \frac{dF(t)}{dt} = \frac{\beta}{\eta} . \left(\frac{t-\gamma}{\eta} \right)^{\beta-1} . \exp\left(-\left(\frac{t-\gamma}{\eta} \right)^{\beta} \right)$$

and instant failure rate λ(t) is given by

$$\lambda(t) = \frac{\beta}{\eta} . \left[\frac{t-\gamma}{\eta} \right]^{\beta-1}$$

If β<1, the failure rate decreases with time.
If β=1, the failure rate is constant and
If β>1, the failure rate increases with time.

WEIBULL'S MODEL AND WAYNE-NELSON METHOD

Hazard rate h(t) is expressed as:

$$h(t) = \frac{1}{1-F(t)} . \frac{dF(t)}{dt} = \beta \frac{(t-\gamma)^{\beta-1}}{\eta^{\beta}}$$

and the cumulative hazard function is written:

$$H(t) = \int_0^t h(t)dt = \frac{(t-\gamma)^{\beta}}{\eta^{\beta}}$$

Note:
In the general case, parameter γ is void. If γ is non-void, there is an origin offset, and the points present a curve with downward facing concavity.

Stress affected at time T is given by:

$$T = n\left[\log \frac{k}{k-1} \right]^{1/\beta} + \gamma$$

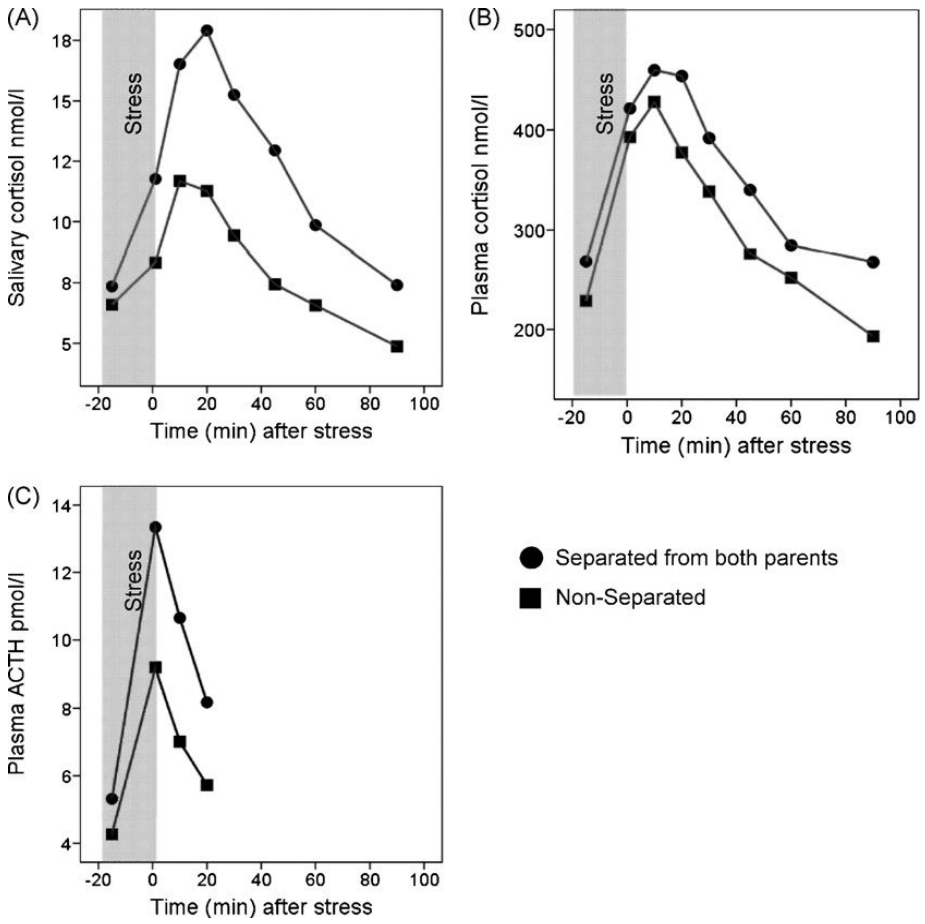
And the percentage *p* of stress corresponds to Time T is calculated by:

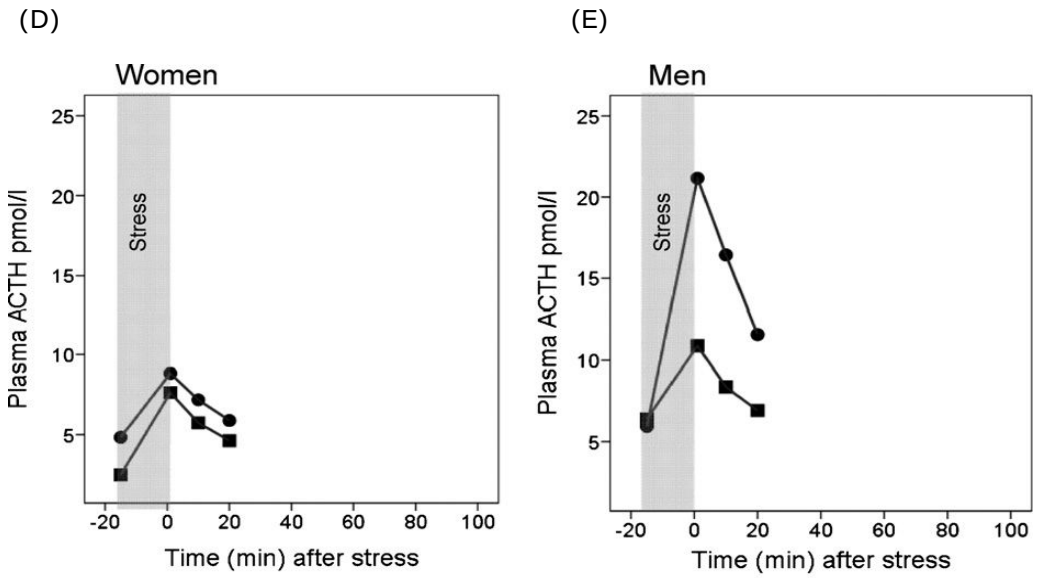
$$p = 1 - \exp\left(-\left(\frac{T_p - \gamma}{\eta} \right)^{\beta} \right)$$

APPLICATION

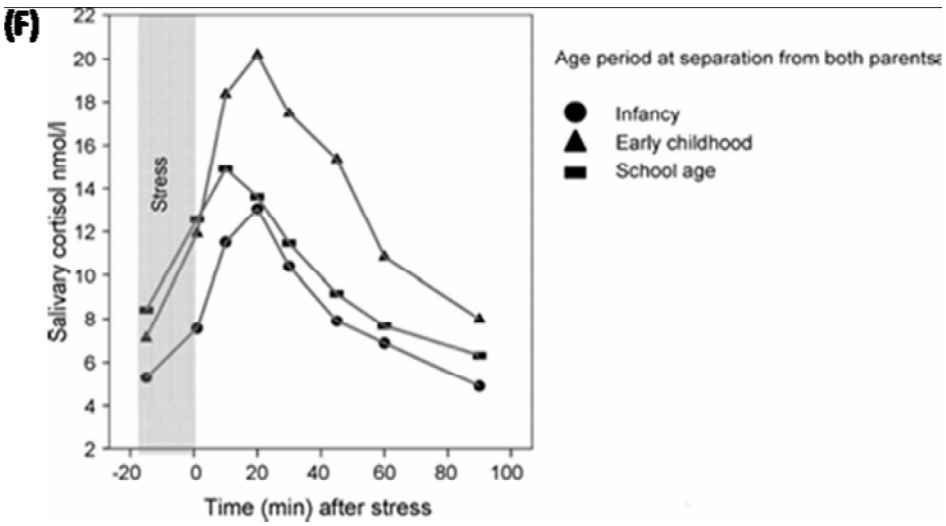
Participants separated from both parents had higher salivary cortisol and plasma ACTH concentrations across all time points compared to non-separated group. They also had higher salivary cortisol reactivity to the stress. Separated men had higher reactivity in response to stress. The effects on the HPA axis were found to differ substantially between genders. Men and Women separated from both parents differed from the non-separated parents.

The following figures (From Fig. A to Fig. E) show the effects of Salivary cortisol, Plasma cortisol , Plasma ACTH for separated and non-separated parents and ACTH concentrations for Women and Men.





The following figure (Fig. F) illustrates the finding by showing salivary cortisol concentrations during the stress in three age groups. Participants separated in infancy (<2 years) and at school age (≥ 7 years) had lower peaks after stress in comparison to participants separated during early childhood (≥2 years and <7 years). Duration of separation had no association with the hormonal responses independently of the age at separation.



DISCUSSION

We have shown that ELS is associated with altered responsiveness of the HPA axis more than 60 years after childhood separation. In comparison to non-separated participants, individuals separated from both parents had higher salivary cortisol and

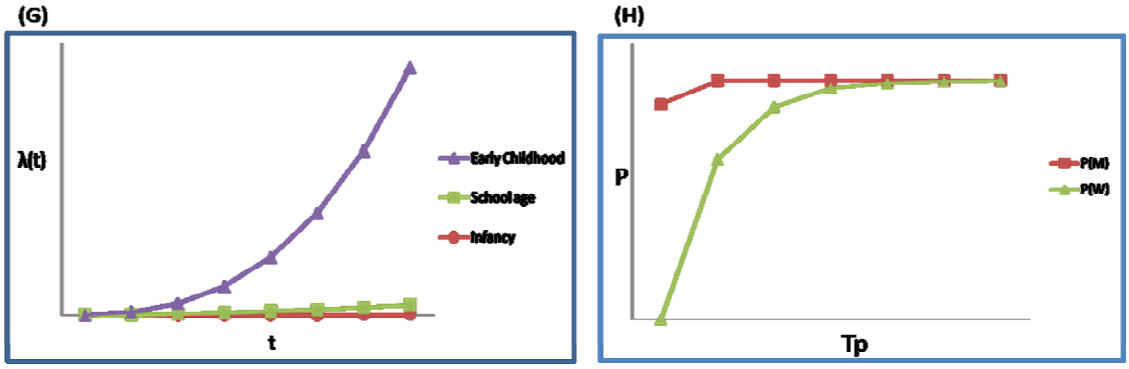
plasma ACTH levels across the time points during the stress and higher salivary cortisol reactivity in response to stress more than 60 years later. Our findings also indicate that the association between a childhood traumatic event and HPA axis function is not explained by the presence of symptoms of depression, which are more common in people who experienced ELS (Pesonen *et al.,* 2007a). This suggests that the interrelations between early life stress, stress physiology, and mental health are not merely due to symptoms of depression. Comparison of our findings with those of (Heim *et al*., 2008) showing that the highest ELS related HPA axis reactivity was observed among men.

The percentage of stress obtained by using Weibull's Model and Wayne-Nelson's method shows the secretion of plasma ACTH is higher for Men who are separated from both parents than from Women who are separated from both parents. It is clear that the secretion of salivary cortisol is more for separating parents than from non-separating parents. According to age at separation from both parents, the hazard rate is more for children separated between 2 and 7 years of age (Early childhood) than the Infancy (before 2 years of age) and School age (after 7 years of age).

RESULT

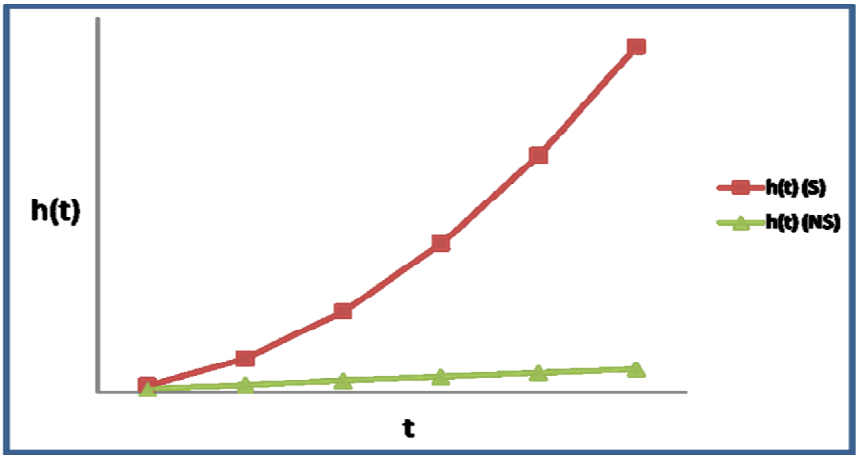
Stress affected time 'T' for (i) Infancy = 2.5 m (ii) Early childhood = 2.5 m (iii) School age = 3 m

The following graph (Fig. G) shows the hazard rate for Infancy (●), Early childhood (▲) and School age (■). And the graph (Fig. H) gives percentage of stress for Women [P(W)] and Men [P(M)].



The following graph (Fig. I) shows the secretion of Salivary cortisol for Non-Separated (NS) and Separated (S) from both parents.

(I)



CONCLUSION

Separation from parents during childhood may alter an individual's stress physiology much later in adult life (i.e.) Early life stress may induce alterations in individual stress physiology that last over the life course.

The Hazard rate graph shows the secretion is higher for salivary cortisol for the participants separated from both parents than from the non-separated parents and the plasma ACTH concentrations for both men and women is higher than from non-separated parents.

The Failure rate graph of salivary cortisol shows that the participants who had experienced the separation in early childhood were more affected than children separated during Infancy or School age.

The Percentage of stress level shows that the Separated men had higher reactivity than women.

The maximum stress levels are experienced by the Children who got separated during their ages between 2 and 7 years.

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