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Exponentially Distributed Outages of Decreased ACTH and Cortisol Responses to Stress in Healthy Adults with Childhood Maltreatment

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ABSTRACT
Preclinical research findings suggest that exposure to stress and concomitantly hypothalamus-pituitary-adrenal (HPA) axis activation during early development can have permanent and potentially deleterious effects. A history of early-life abuse or neglect appears to increase risk for mood and anxiety disorders. Abnormal HPA response to stress challenge has been reported in adult patients with Major Depressive Disorder and Post-Traumatic Stress Disorder. This paper discussed the constant stress level of adult patients with times to damage of stress effect and recoveries**.** Also In adults without diagnosable psychopathology, childhood maltreatment is associated with diminished HPA axis response to a psychosocial stressor.
Keywords-HPA Axis, Cortisol, ACTH, stress level, TTO, TTP.

I. INTRODUCTION

Cortisol dysregulation and deficient glucocorticoid feedback regulation have been identified as biological correlates of adult depression and anxiety disorders, and early life adversity is consistently associated with these disorders in epidemiological studies. A large body of clinical literature has characterized major depressive disorder (MDD) as a condition associated with excessive basal cortisol secretion and inadequate inhibitory feedback regulation of the hypothalamus-pituitary-adrenal (HPA) axis constituents[4]. Conversely, relatively low basal cortisol concentrations, low awakening cortisol response, and enhanced cortisol suppression following low-dose dexamethasone administration have been suggested as correlates of Post-Traumatic Stress Disorder (PTSD).

An established risk factor for depression was found to be associated with suppressed ACTH and cortisol responses to a standardized laboratory stressor (i.e., theTrier Social Stress Test) in a sample of healthy adult subjects, though a significant positive relationship between cortisol response and inhibited temperament has also been seen in healthy adults. Childhood maltreatment, another risk factor for depression, has recently been examined in nonclinical samples[5]. Women with a history of sexual or physical abuse demonstrated increased ACTH but normal cortisol responses to the TSST when compared with female control subjects without abuse histories.

Also here the ACTH and cortisol responses to a standardized laboratory stress test in healthy adults without MDD or PTSD is described. A group reporting a history of moderate to severe childhood maltreatment in the form of neglect or abuse was compared with a group reporting none. Based on the work examining cortisol response to the dexamethasone/corticotropin releasing hormone (Dex/CRH) test as a function of perceived early life stress, implied that increased cortisol response would be detected among healthy individuals reporting a history of childhood trauma[6,7].

II. METHODS

Plasma adrenocorticotropin (ACTH) and cortisol reactivity to the Trier Social Stress Test were examined in healthy adults (N=50) without current psychopathology. Subjects with a self reported history of moderate to severe childhood maltreatment (MAL; n=23) as measured by the Childhood Trauma Questionnaire were compared with subjects without such a history (CTL; n=27). Fifty adults, ages 20 to 59, were selected for participation by Advertisements for "healthy adults with a history of early life stress". The persons are included only those who scored "moderate" to "severe" on at least one of the five subscales of the Childhood Trauma Questionnaire (CTQ;) and did not meet current DSM-IV criteria for MDD or PTSD (n=23). the healthy volunteers (n=27) were recruited via advertisements for "healthy research subjects." They were selected only those who generated a categorical score of "none" on all five CTQ subscales and were similarly free of current MDD and PTSD. All subjects were free of pregnancy, significant medical illness and recreational drug use as evidenced by complete

physical and neurological examination, standard laboratory tests, and Electrocardiogram.

Notations

A- Steady-state system availability
λ- Rate of failures (unplanned outages)
μ- Repair rate for unplanned outage
μ_2-Upgrade rate for planned outage
T-Time to damage of cortisol and ACTH level.
TTP-Time to planned outage

III. APPLICATION

A history of early-life abuse or neglect appears to increase risk for mood and anxiety disorders. Abnormal HPA response to stress challenge has been reported in adult patients with Major Depressive Disorder and Post-Traumatic Stress Disorder[1]. Cortisol dysregulation and deficient glucocorticoid feedback regulation have been identified as biological correlates of adult depression and anxiety disorders, and early life adversity is consistently associated with these disorders in epidemiological studies. A large body of clinical literature has characterized major depressive disorder (MDD) as a condition associated with excessive basal cortisol secretion and inadequate inhibitory feedback regulation of the hypothalamus-pituitary-adrenal (HPA) axis constituents. Conversely, relatively low basal cortisol concentrations, low awakening cortisol response , and enhanced cortisol suppression following low-dose dexamethasone administration have been suggested as correlates of Post-Traumatic Stress Disorder (PTSD). Childhood maltreatment, another risk factor for depression, has recently been examined in nonclinical samples. Women with a history of sexual or physical abuse demonstrated increased ACTH but normal cortisol responses to the TSST when compared with female control subjects without abuse histories. Compared with CTLs, MAL subjects a significant group effect was seen in the cortisol response to the stress challenge, reflecting lower concentrations among MAL subjects and also a significant group × time effect characterized the relatively blunted ACTH response of the MAL group. Emotional Neglect and Sexual Abuse strongly predicted maximal cortisol release.

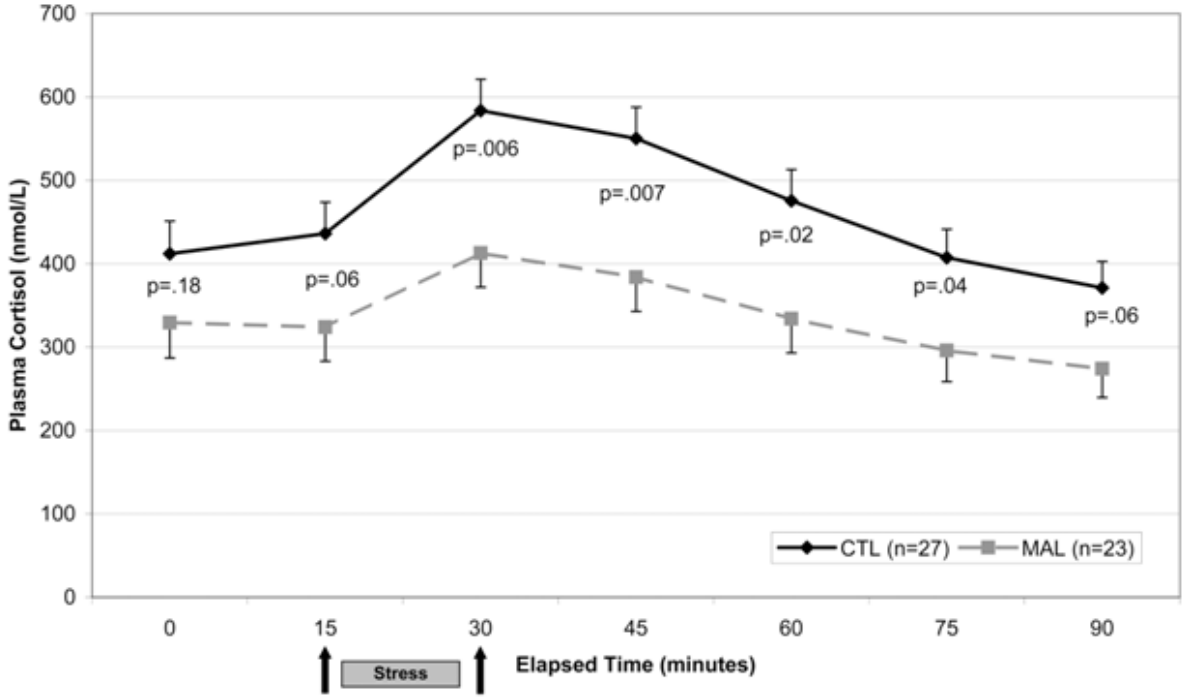


Fig 1.

Plasma cortisol response to Trier Social Stress Test in Healthy Adults with (n=23) and without(n=27) a history of childhood maltreatment. A significant main effect of group is present F=5.9[1], p=.02. P-values reported on the graph represent group differences at individual time points.

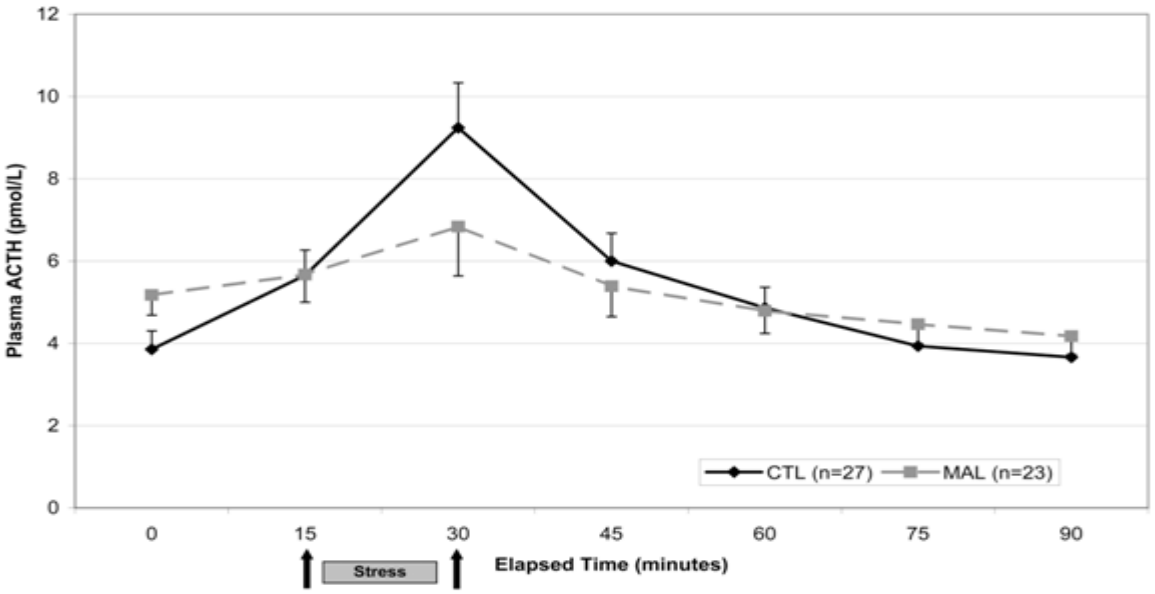


Fig 2:

Plasma ACTH Response To Trier Social Stress Test. Repeated Measures Analysis Showed a significant Within-Subjects Interaction Of Abuse × Time (F=4.3[1.6], P=.02). Analysis Of individual Time Points Revealed None With Significant Group Difference.

IV. METHODS

Plasma adrenocorticotropin (ACTH) and cortisol reactivity to the Trier Social Stress Test were examined in healthy adults (N=50) without current psychopathology. Subjects with a self reported history of moderate to severe childhood maltreatment (MAL; n=23) as measured by the Childhood Trauma Questionnaire were compared with subjects without such a history (CTL; n=27). Fifty adults, ages 20 to 59, were selected for participation by Advertisements for "healthy adults with a history of early life stress". The persons are included only those who scored "moderate" to "severe" on at least one of the five subscales of the Childhood Trauma Questionnaire (CTQ;) and did not meet current DSM-IV criteria for MDD or PTSD (n=23). the healthy volunteers (n=27) were recruited via advertisements for "healthy research subjects." They were selected only those who generated a categorical score of"none" on all five CTQ subscales and were similarly free of current MDD and PTSD. All subjects were free of pregnancy, significant medical illness and recreational drug use as evidenced by complete physical and neurological examination, standard laboratory tests, and electrocardiogram.

Mathematical model

The steady-state availability of the system in this section can be obtained from the general formula[2,3].

$$A = [\ 1+\frac{\lambda}{\mu}+\frac{\lambda}{\mu_2}\cdot\frac{\alpha(\lambda)}{1-\alpha(\lambda)}\ ]^{-1}$$
$$= [\ 1+\frac{\lambda}{\mu}+\theta(\lambda)\ \cdot\ \frac{\lambda}{\mu_2}\ ]^{-1}$$

$$\alpha(\lambda) \equiv \int_0^{\infty} \exp(-\lambda.x)\, dF(x)$$

$$\theta(\lambda) \equiv \frac{\alpha(\lambda)}{1-\alpha(\lambda)}$$

Now, the Availability formula for the distribution of TTP is exponentially distributed.

Let TTP = T,

Also,let

F(x)≡1-exp(-x/T),T>0,x>0

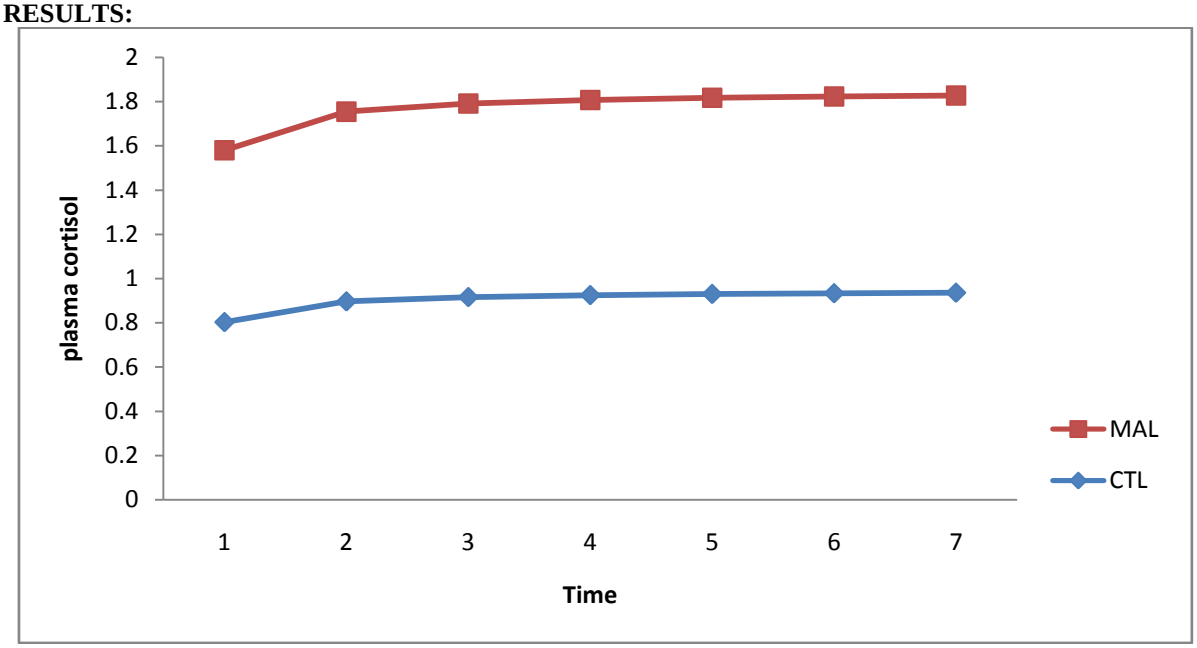
T=MTTP,λ_2=1/T;

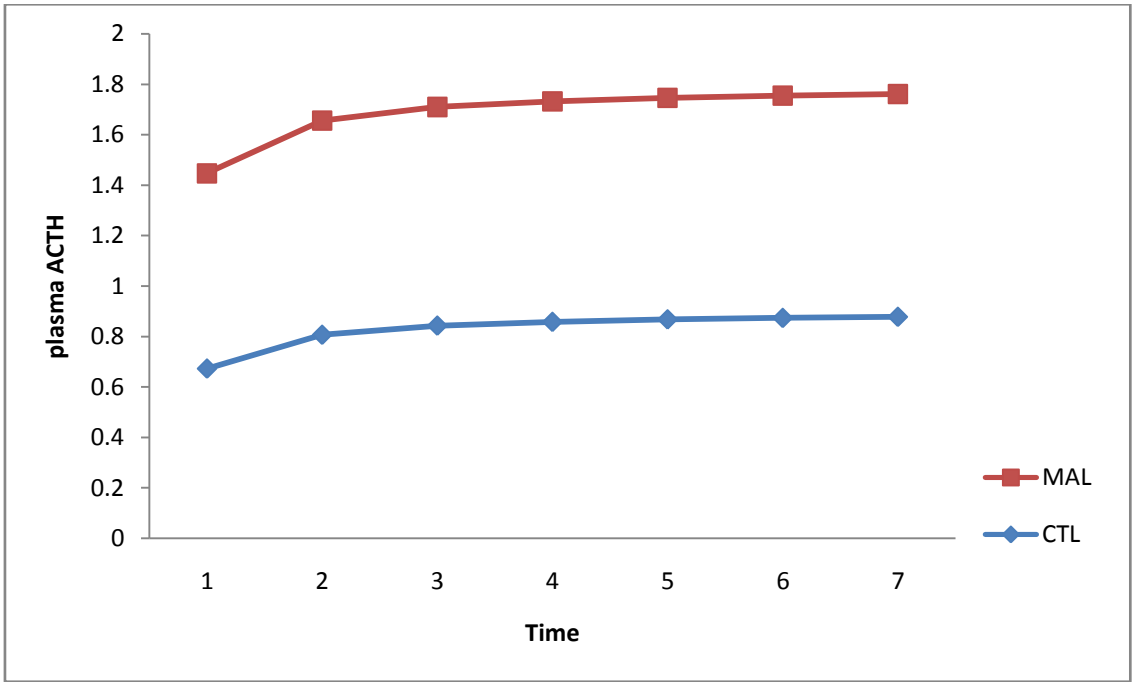
Now, $A_E(T)=[1+\frac{\lambda}{\mu}+\frac{1}{\mu_{2.T}}]^{-1}$

TABLE: 1

	CTL					MAL				
	□	μ	μ_2	T	$A_D(T)$	□	μ	μ_2	T	$A_D(T)$
CORTISOL	0.241	4.421	6.525	0.8	0.8025	0.340	3.139	7.049	0.8	0.7778
				2.5	0.8962				2.5	0.8583
				4.1	0.9158				4.1	0.8750
				5.7	0.9247				5.7	0.8825
				7.4	0.9300				7.4	0.8869
				9	0.9332				9	0.8896
				10.7	0.9356				10.7	0.8916
ACTH	0.350	3.208	2.944	0.9	0.6727	0.357	2.997	6.542	0.9	0.7744
				2.6	0.8066				2.6	0.8490
				4.4	0.8429				4.4	0.8667
				6	0.8578				6	0.8737
				7.8	0.8676				7.8	0.8782
				9.5	0.8735				9.5	0.8809
				11.3	0.8778				11.3	0.8829

RESULTS:





V. CONCLUSION

A history of early-life abuse or neglect appears to increase risk for mood and anxiety disorders. Abnormal HPA response to stress challenge has been reported in adult patients with Major Depressive Disorder. In adults without childhood maltreatment is associated with diminished HPA axis response to a psychosocial stressor. Also found the steady state availability of exponentially distributed model of cortisol, ACTH levels due to stress.

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