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Mathematical Model for the Effects of Age and Gender on Pituitary – Adrenocortical Responsiveness in Humans

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ABSTRACT
In the present paper, we discuss the methods of determining the reliability of the system, when we have information on the reliability of its subsystems (or) components. The reliability function is a function of time, R(t), $0 < t < \infty$. The time t is fixed at a given value say t_0. So, we express the reliability of the system, R_{sys} as a function $\psi(R_1, R_2, \ldots\ldots\ldots R_n.)$ of the reliability values of its subsystems. In the application part we consider, the human system and HPA as its sub system. The values for cortisol and ACTH for young men, oldmen, young women, old women are compared (i) when CRH alone is administered (ii) when CRH + AVP combined is administered. MTTF values are obtained for all the four cases. Even though, the time is small, the fractions show a high degree of intraindividual constancy overtime which proves the medical report. The results in medical model suggest that at least in men, an impaired feed back inhibition of pituitary adrenal secretory activity contributed to the age induced increment in pituitary adrenal responsiveness.
Keywords : Cortisol, ACTH, CRH, CRH / VP.
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I. MATHEMATICAL MODEL

We discuss methods of determining the reliability of a system when we have information on the reliability of its subsystems or components and we know the structure of the system. The reliability is a function of time R(t), $0 < t < \infty$.

Consider a system having two components C_1 and C_2. We say that the two components are connected in series if the failure of either one of components causes an immediate failure of the system.

Let I_i (i = 1, 2) be an indicator function, assuming the value $I_i = 1$ if component C_i operates throughout the specified period $[0, t_0)$, and $I_i = 0$ otherwise. The system operates through the period $[0, t_0)$ if and only if $I_1I_2 = 1$; We therefore define the series structure function,

$\psi_s(I_1, I_2) = I_1 . I_2$ →(1.1)

Both I_1 and I_2 are random variables and $E\{I_i\}= Pr \{ I_i =1\}= R_i$, where E{.}denotes the expected value and R_i is the reliability of C_i, i = 1, 2. Notice that $\psi_s (I_1, I_2)$ assumes only the value 0 (if the system fails) or 1 (if the system survives). The reliability of the system is

$R_{sys} = Pr\{\psi_s(I_1, I_2) = 1\}$ → (1.2)
$= Pr\{ I_1 = 1; I_2 = 1\}$

But due to the independence of I_1 and I_2,
$Pr\{ I_1 = 1, I_2 = 1\}= Pr\{ I_1 = 1\}Pr\{ I_2 = 1\}$
Hence

$R_{sys} = R_1. R_2$ →(1.3)

Thus, if we define the function $\psi_s(x_1,x_2)=x_1.x_2$, for all x_1,x_2 in [0,1]
Then

$R_{sys} = Pr\{\psi_s (I_1, I_2)=1\}$
$=\psi_s(R_1,R_2)$ →(1.4)

We can extend this result to a system of n independent components connected in series. Thus, let

$\psi_s(x_1,\ldots..x_n) = \prod_{i=1}^{n} xi$ →(1.5)

for all x_i in [0,1], where

$\prod_{i=1}^{n} ai = a_1, a_2, \ldots a_n$

Then

$R_{sys} = Pr \{\psi_s(I_1,I_2,I_3\ldots I_n)=1\}$
$= R_1R_2 \ldots. R_n$ →(1.6)
$= \psi_s (R_{1,,} \ldots R_n)$

Notice that if $T_1,\ldots. T_n$ are the actual failure times of the n components, then the failure time of a system connected in series is

$T_s = \min T_i$
$1 \le i \le n$

A system of two components, C_1 and C_2 is connected in active-parallel if the system fails only when both components fail. The parallel structure function is

$\psi_p (x_1,x_2) = 1 – (1 – x_1) (1 – x_2)$ → (1.7)

$0 \le x_1, x_2 \le 1$. In terms of the indicator functions I_1 and I_2,

$\psi_p (I_1,I_2)= 1 – (1 – I_1) (1 – I_2) = I_1 + I_2 – I_1 I_2$ → (1.8)

Thus $\psi_p (I_1, I_2) = 0$ iff both $I_1 = 0$ and $I_2 = 0$. In this case, if I_1 and I_2 are independent,

$R_{sys} = Pr \{\psi_p (I_1, I_2) = 1\} = 1 - E \{1 - I_1\} E \{1 - I_2\}$
$= 1 - (1 - R_1) (1 - R_2) = \psi_p (R_1, R_2)$

If the system is comprised of n independent components, connected in active parallel, then

$$R_{sys} = \psi_p (R_1,\ldots R_n) = 1 - \prod_{i=1}^{n} (1 - R_i)$$

When Cortisol (100µg CRH alone) is given to youngmen ,

$R_{sys} = 1- [(1- R_1) (1 - R_2) (1 - R_3) (1 - R_4) (1 - R_5) (1 - R_6)]$

$R_{sys} = 0.9999$

Similarly, for other cases also $R_{sys} = 0.9999$

II. APPLICATION

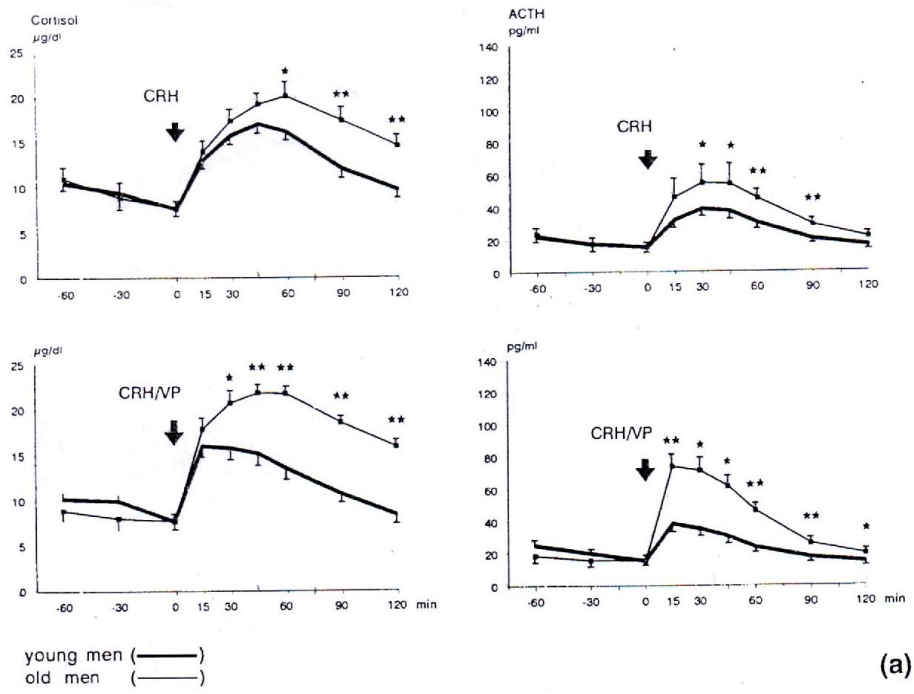
Aging appears to be accompanied by a progressive disturbance of the hypothalamus pituitary – adrenal (HPA) system which is the most important mediator of the neuro-endocrine response to stress [12]

However there is growing evidence from animal studies that age-dependent dysfunctioning of the HPA system is not restricted to the hippocampus and hypothalamus but occurs also at the pituitary level. Also, two human studies have reported [7,8] on a tendency towards enhanced peak ACTH and cortisol concentrations following administrative of ovine CRH in healthy elderly compared to younger controls.

Contrasting with the rather inconsistent findings after stimulation solely with CRH, substantially elevated responses of ACTH and cortisol were found in the healthy elderly when stimulated with a combined bolus injection of hCRH and vasopressin (VP) [2].

Vasopressin is besides CRH, the most important secretgogue for ACTH [1,3,13]. Hence, the combined administration of both peptides appears to be more physiological test of pituitary-adrenal functioning.

The effect of gender on pituitary adrenal activity is even less well investigated than that of age, although a distinct dependency on the sex is well known for the release of some other pituitary hormones [4]. Thus, in humans cortisol secretion during the 24-h cycle did not differ significantly between the sexes, but ACTH secretion was higher in men than in women [4]. The present study aimed to distinguish the effects of age and gender on pituitary-adrenal responsiveness to hCRH alone and to a combined injection of hCRH and Vasopressin



(a)

Plasma cortisol (left) ACTH (right) concentrations prior to and after stimulation with 100µg of human corticotropin releasing hormone (hCRH) alone (upper panels) and a combination of hCRH (100 µg) and arginine vasopressin (VP 0.5 IU); lower panels: (a) in young (thick solid) and old men (thin solid) (b) in young (thick dashed) and old women (thin dashed)

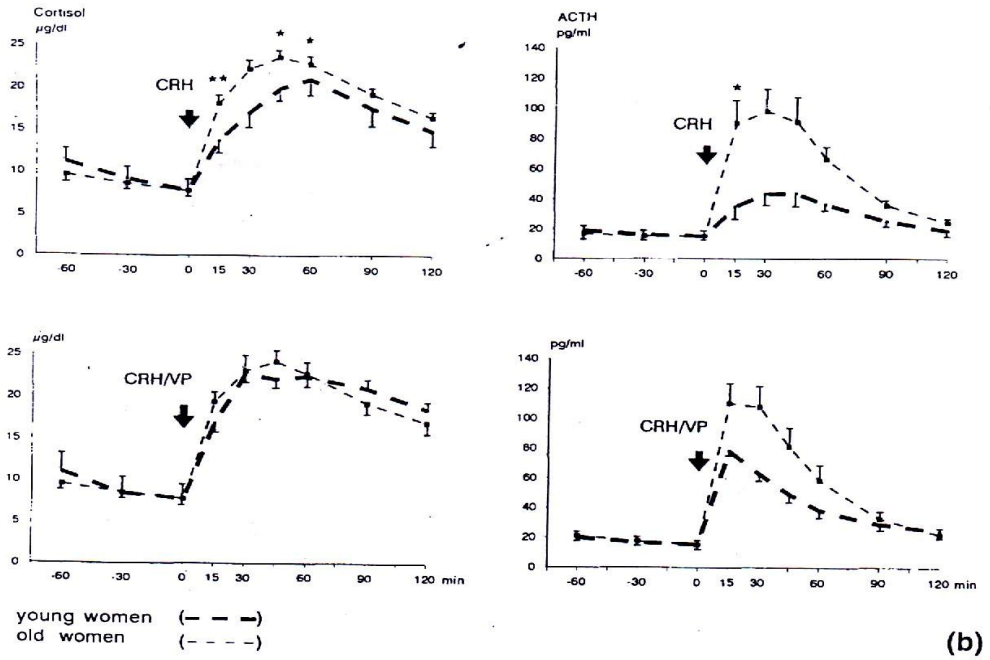
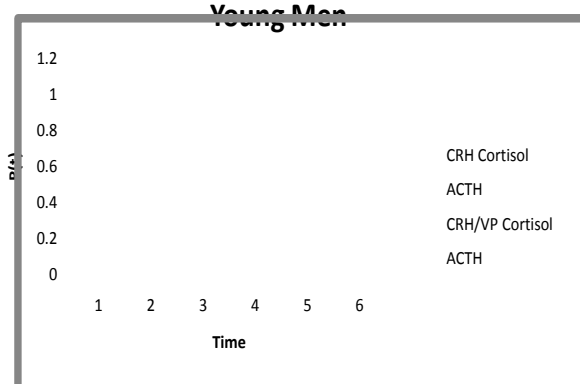


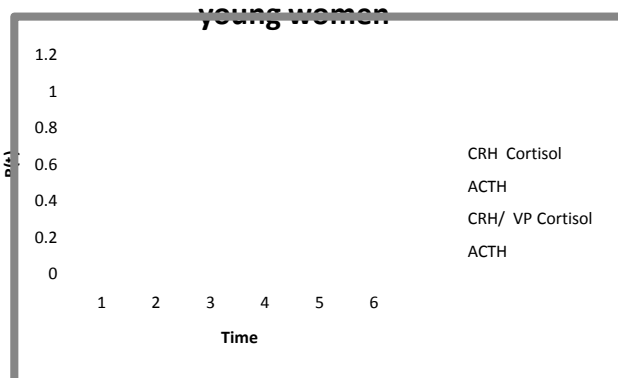
Fig. 1 (cont.)

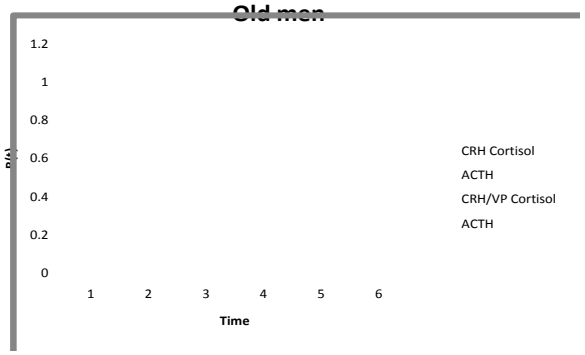
III. MATHEMATICAL RESULTS

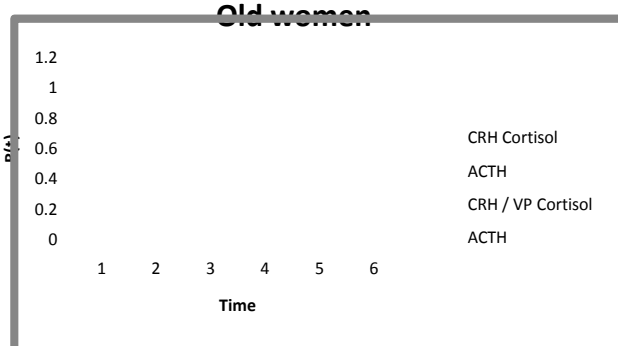
By using the formula R(t) = $\exp\left[-\left(\frac{t-t_0}{\theta}\right)^{\beta}\right]$, $t \geq t_0$

We get the following figures









IV. MEAN TIME TO FAILURE FUNCTION

$$MTTF = t_0 + \theta\ \Gamma\left(1+\frac{1}{\beta}\right)$$

MTTF values for young men

Group	Cortisol	ACTH
CRH	3.9723	4.8694
CRH + VP	3.9740	4.1321

MTTF values for old men

Group	Cortisol	ACTH
CRH	4.001	4.2098
CRH + VP	4.0209	4.054

MTTF Values for young women

Group	Cortisol	ACTH
CRH	3.9883	4.58
CRH + VP	3.9923	4.1335

MTTF values for old women

Group	Cortisol	ACTH
CRH	4.0187	3.9577
CRH + VP	4.0138	3.9572

V. CONCLUSION

The reliability to test the effect of cortisol and ACTH are measured and compared with the mathematical model. Basal secretion of cortisol did not differ among groups. But basal concentrations of ACTH were diminished in young women. Pituitary responses to hCRH did not differ between young men and women. However , responses to hCRH/VP were stronger in the younger females. Pituitary – adrenal secretory responses were greater in old than in young men after sole injuction of hCRH and even more so after combined injection of hCRH/VP. In old women, pituitary adrenal secretory responses were also greater than in young women. But, in particular for responses to hCRH/VP, the effects were less distinct than within the men. From the mathematical model, the values for cortisol and ACTH for young men, old men,. young women, old women are compared (i) when CRH alone is administered . (ii) when CRH and AVP combined is administered. MTTF values are obtained for all the four cases. Even though the time is small, the fractions show a high degree of intra individual constancy overtime,which proves the medical report. The results in medical model suggest that atleast in men, an impaired feed back inhibition of pituitary adrenal secretory activity contributed to the age induced increment in pituitary adrenal responsiveness.[9,10,11]

REFERENCES

[1] Axelrod J . Reisine TD. Stress hormone: their interaction and regulation . Science 1984: 224:452- 459

[2] Dodt C.Dittmann J . Hruby J. Spath-Schwalbe E. Born J. Schutler R. et al. Different regulation of adrenocorticotropin and cortisol secretion in young. Mentally healthy elderly and patients with senile dementia of Alzheimer's type. J Clin Endocrinol Metab 1991:72:272-276.

[3] Familari M. Smith AI. Funder JW, Arginine vasopressin is a much more potent stimulus to ACTH release from ovine anterior pituitary cells than ovine corticortropin releasing factor. Neuro endocrinology 1989:50:152-157

[4] HO KY. Evans WS. Blizzard RM. Effects of sex and age on the 24 hour profile of hormone secretion in man: importance of endogenous estradiol concentrations. J Clin Endocrionol Mctab 1987: 64:51-58

[5] Lakshmi. S and Shanmaga priya.S, Mathematical model for the Corticosteroid feed back effects on ACTH secretion in hypoadrenocorticism . Acta Ciencia Indica, 2008 Vol . XXX IV M, No.4 1767

[6] Lakshmi.S and Senthil Kumar. P Stochastic model for cortisol secretion due to human stress in journal of Indian Acad Math,(2007) Vol 29, No. 2 PP. 313-321

[7] Ohashi M. Fujio N. Kato K. Nawata H. Iharyashi H. Aging is without effect on the pituitary – adrenal axis in men . Gerontology 1986:32:335-339 .

[8] Pavlov EP. Harman SM. Chrousos GP. Loriaux DI,. Blackman MR . Responses of plasma adrenocorticotropin. Cortisol. and dehydroepiandrosterone to ovine corticotropin-releasing hormone in healthy aging men. J Clin Endocrinol Metab 1986:62:767-772.

[9] Reul JMHM. Rothuizen J. DeKloet ER. Age-related changes in the dog hypothalamic-pituitary – adrenocortical system: Neuroendocrine activity and corticosteroid receptors. J Steroid Biochem Mol Bio1991:40:63-69.

[10] Sapolsky RM. Krey LC. McEwen BS.The neuroendocrinology of stress and aging: the glucocorticoid cascade hypothesis. Endocr Rev 1986:77: 284-304

[11] Sapolsky RM, Krey LC. McEwen BS. Glucorticoid sensitive hippocampal neurons are involved in terminating the adrenocortical stress response.Proc Natl Acad Sci USA 1984:81: 6174-6177 .

[12] Selye H. Tuchweber B. Stress in relation to aging and disease. In Everitt A. Burgaes J. editors. Hypothalamus. pituitary and aging . Springfield.II: Charles C Thomas 1976:557-573 .

[13] Spath - Schwalbe E. Fehm HL. Born J. Pfeiffer EF. Combined corticotropin releasing hormone vasopressin test: a new test for the evaluation of the pituitary adrenal system. Horm Metab Res 1987: 19: 665-666.