RESEARCH ARTICLE   OPEN ACCESS

Cumulative hrf of NMWD model for Renin in patients with Depression

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Abstract :
Hypercortisolism as a sign of hypothamamus-pituitary-adrenocortical (HPA) axis over activity and sleep EEG changes are frequently observed in depression. Closely related to theHPA axis is the renin-angiotensin-aldosterone system (RAAS) as 1. adrenocorticotropic hormone(ACTH) is a common stimulus for cortisol and aldosterone, 2. cortisol release is suppressed bymineralocorticoid receptor (MR) agonists 3. angiotensin II (ATII) releases CRH and vasopressin from the hypothalamus. Here difference of sleep related activity of the RAAS between depressed patients and healthy controls and also we found the analysis of survival function and cumulative hazared rate function for renin.
Keywords: Cumulative hrf, NMWD , depression

I.   Introduction:

Hypercortisolism as well as a reduced feedback inhibitionof the hypothalamus-pituitary-adrenocortical (HPA) systemare frequently observed in depression [1]. Further,a decreased ability of dexamethasone to suppress adrenocorticotropichormone (ACTH) and cortisol secretion isfound in depressed patients, but appears to depend on theclinical characteristics, especially "typical" vegetativesigns, as sleep disturbances and weight loss [2,3] andreproductive state in females . A reduced plasma renin activity(PRA) indepressed patients [4] and an increase in restingPRA accompanied by a blunted renin response to posturein bipolar patients. The latter study described a normalaldosterone concentration, which was interpreted tobe inappropriately low in relation to the increased PRA. Apossible link between possible changes of the RAAS andthe HPA system in depression was further demonstratedby the significant increase in aldosterone secretion afteradministration of the glucocorticoid receptor agonist dexamethasonein healthy female subjects, whereas indepressed females aldosterone showed a trend to a decrease.

Methods: We studied nocturnal plasma concentration and sleepEEG in 7 patients with depression(1) male, 6 females, age:53.3 ± 14.4 (mean ± SD), range 34 – 70 years) and 7 agematched controls (2) males, 5 females, age: 54.7 ± 19.5,range 27 – 76 years). The data from three of the controlswere derived from the control condition of an earlierstudy [5] and four were newly recruited. Both patientsand controls were free of medication for at least 10 daysand for fluoxetine for at least 4 weeks with the exceptionof 1 patient receiving 500 mg chloral hydrate at the twostudy nights and one subject receiving metoclopramid 10mg once the day of the examination. However, evenafter exclusion of these subjects the main findings of thestudy were unchanged (data not shown). No substancesfor blood pressure regulation, especially beta-receptorblockers or angiotensin-converting enzyme inhibitors ordiuretics were used by any of the subjects. Further no relevantcomorbidity, especially no cardiovascular, renal orhepatic disorder was present in the patients or controls, asassessed by clinical examination and a standard clinicallaboratory examination including serum creatinine and liver enzyme levels. The personal and family history of thecontrols was free of psychiatric disorders.
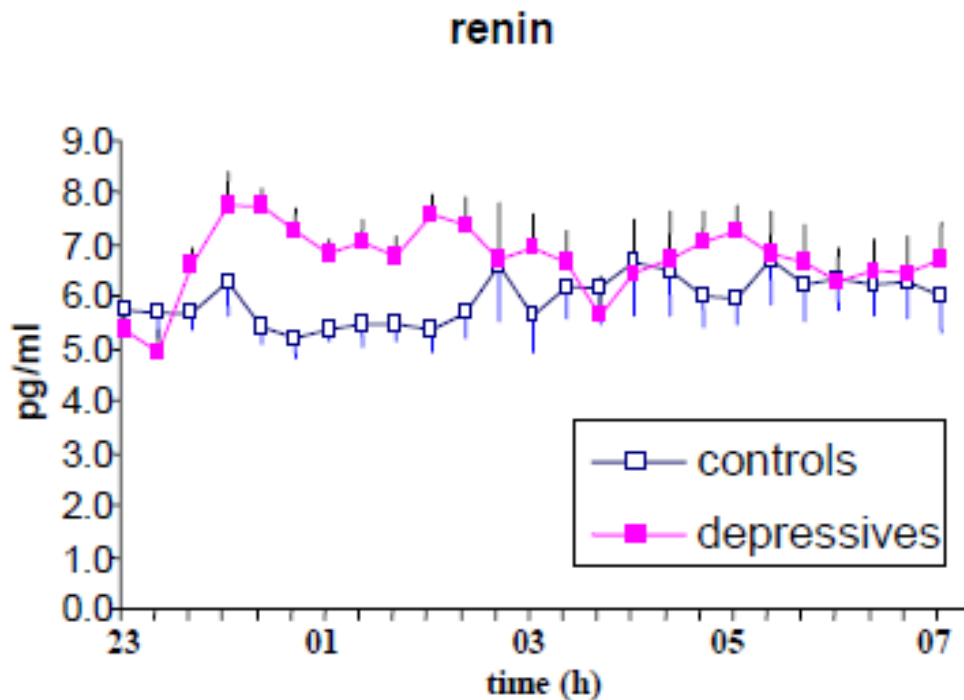
Geetha.T Int. Journal of Engineering Research and Applications
ISSN : 2248-9622, Vol. 4, Issue 11(Version - 6), November 2014, pp.151-153

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Figure 1 : Time Course of renin hormone secretion in patients with depression compared to controls (mean ± SEM)

II.   Mathematical Model :

Acronyms

hrf   – Hazard Rate Function
NMWD – New modified Weibull distribution
sf   – Survival Function

Notations

a,b   - NMWD parameters a>0,b>0 for renin
h(t)   – hrf of renin
H(t)   – cumulative hrf of renin
t   – time of renin
$\bar{F}$(t)   – sf of renin

Here,The usual 2-parameter Weibull distribution can be specified through its Sf:

$\bar{F}(t;\beta,\lambda) = \exp[-(\lambda .t)^{\beta}]$ --- ----------- ---------------- (1)

The lifetime distribution for NMWD arises from taking appropriate limits on the Beta integrated distribution from [6] The Sf is

$\bar{F}(t;\beta,\lambda) = \exp[- a .t^{b} .(\lambda .t)]$ ----------- ------------------ (2)

With parameters a > 0, b ≥ 0 and λ > 0.

The pdf and hrf are:

f(t) = a . (b + λ . t) .t $^{b-1}$ .exp (λ .t) . exp [-a . t^{b} .exp (λ.t)] ----------(3)

h(t) = a . (b + λ . t) .t $^{b-1}$ .exp (λ .t) --- --------(4)

The derivative of h(t) intersects the t axis only once, at t* for t>0.h(t) is decreasing for
 t < t*,and is increasing for t > t* which is given by

$t^* = \frac{\sqrt{b}-b}{\lambda}$ ----------------------- --------------------(5)

The interesting feature is that t* decreases as λ increases.

For λ = 0 in (2) NMWD reduces to $\bar{F}$(t) = exp [- a .t^{b}] ------------(6)

Which is a common 2-parameter Weibull distribution.

The beta-integrated model was first introduced in [6]. The model's cumulative hrf and sf are:

$H(t) = a.t^{b}.(1 - d.t)^{c}$,   0< t < 1/d ; ---------------(7)

$\bar{F}$(t) = exp[-H(t)];   a,b,d > 0; c < 0 ---------------(8)

Set d=1/n, c=λ.n, For n→∞,

$\left(1 - \frac{t}{n}\right)^{-\lambda.n}$ →exp(λ . t).

and this yields

$H(t) = a \cdot t^b \cdot \exp(\lambda \cdot t).$
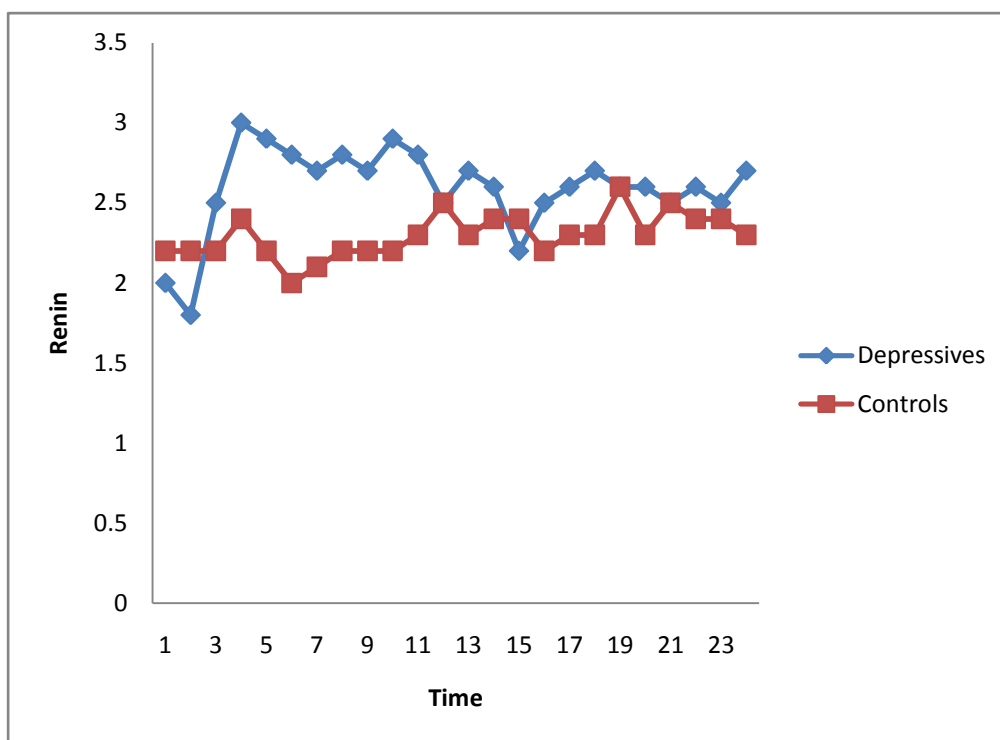
----------------(9)

Which is the cumulative hrf for NMWD.

The data is fitted with the distribution and the corresponding values for case:1 and case:2 are obtained as follows

Case 1: Depressive
If a=2.6887, b=10.2527, t= 0.5 then H(t) = 0, $\bar{F}(t) = 0.9978$
Case 2 : Control
If a=2.3572, b=18.8723, t= 0.5 then H(t) = 0, $\bar{F}(t) = 0.9999$

III. Conclusion:

There was no difference of sleep related activity of the RAAS between depressed patients and healthy controls and also we found the analysis of survival function and cumulative hazard rate function for renin.

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