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STOCHASTIC MODEL TO FIND THE ADRENOCORTICOTROPIC HORMONE ON CORTISOL AND DHEA'S PRODUCTION THROUGH HAMILTON JACOBI BELLMANN EQUATIONS USING NORMAL DISTRIBUTION

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Abstract:

The adrenal glands are the primary source of minerocorticoids, glucocorticoids, and the so called adrenal androgens. Under physiological conditions, cortisol and adrenal androgen synthesis are controlled primarily by ACTH. Although it has been established that ACTH can stimulate steroidogenesis, the effects of ACTH on overall gene expression in human adrenal cells have not been established. In this paper, we estimate the Adrenocorticotropic Hormone on cortisol and Dehydroepiandrosterone Sulfate (DHEA's) production through Hamilton Jacobi-Bellmann equation using stochastic analysis.

Key Words: Adrenocorticotropic Hormone, Cortisol, Dehydroepiandrosterone Sulfate, Hamilton Jacobi Bellmann Equation, Ornstein Uhlenbeck Process & Normal Distribution

1. Introduction:

ACTH is a 39 amino acid polypeptide predominantly synthesized in and secreted from the anterior lobe of the pituitary gland. The synthesis and secretion of ACTH are tightly controlled by the hypothalamic pituitary adrenal axis. Under stress conditions, the paraventricular nucleus of the hypothalamus secretes vasopressin and CRH. These two peptides regulate the anterior lobe of the pituitary gland and stimulate the secretion of ACTH. ACTH subsequently induces adrenal cortex expansion and corticosteroid production (mainly cortisol in humans). Once synthesized, cortisol in turn acts on the hypothalamus and pituitary (To suppress CRH and ACTH production) causing a negative feedback cycle. In the adrenal glands, ACTH acts by binding to specific cell surface ACTH receptors (Melanocortin 2 Receptor MC2R). MC2R is a seven membrane spanning G-protein coupled receptor that is primarily expressed in adrenocortical cells. Upon ligand binding, the receptor undergoes conformational changes that stimulate adenylyl cyclase, leading to an increase in intracellular cAMP and subsequent activation of protein kinase A (PKA).

Although previous studies have identified some ACTH responsive genes that are involved with the steroidogenic and growth related effects of ACTH [1-3], [6-7], [9] & [16], there is a lack of knowledge regarding the global actions of ACTH on gene expression. Given the critical role of ACTH in adrenal development, steroidogenesis, and disease, it is appropriate to further define the detailed effects of ACTH on human adrenal cell gene expression.

In this paper the problem is investigated by using the boundary condition of Halmilton Jacobi Bellman equation [17]. The continuous time portfolio optimization problem in [4]. The sufficient conditions to verify that a solution derived from the Hamilton Jacobi Bellman equation are in fact an optimal solution to the portfolio selection problem. Many studies have been done on continuous time portfolio optimization problem with the Merton's seminal work [8] & [19-20]. In particular, there has been increasing interest in finding an optiomal portfolio strategy when investment opportunities are stochastic, because many empirical works conclude that investment opportunities are time-varying. There are two main approaches in solving continuous time portfolio optimization problem. One is the stochastic control approach and the other is the martingale approach. In the stochastic control approach, an optimal solution is conjectured by guessing a solution to the HJB equation. It is necessary to verify that the conjectured solution is in fact solution to the original problem. In [5] pointed out, the verification is often skipped since it is mathematically demanding for Kim and Omberg examined the finiteness of conjectured value function very carefully, but they could not provide verification conditions. The sufficient condition to verify that the conjectured solution is in fact the solution to the original problem.

2. Stochastic Model:

Let (ψ, D, P) be a complete probability space on which we define a two-dimensional standard Brownian motion $B = (B^1, B^2)^T$ and we also fix a time interval $[0, T]$. Let $D(t)$ be the augmentation of the filtration $D^B(t) := \omega(B(a); 0 < a < t)$, $0 < t < T$.

Let Y be an Ornstein Uhlenbeck process:

$$dY(t) = \alpha(\bar{Y} - Y(t))dt + \omega_Y\left(\beta dB^1(t) + \sqrt{1-\beta^2}\,dB^2(t)\right) \quad (1)$$

$$Y(0) = y_0 \in \square .$$

$\beta \in [-1,1], \alpha > 0, \omega_Y > 0, and \bar{Y} \in \square$. We call Y a state process, because it determines an investment opportunity set in our portfolio problem. There is one riskless asset and one risky asset. Suppose the price A_0 of the riskless asset satisfies $dA_0(t) = qA_0(t)dt, A_0(0) = 1,$

Where $q \geq 0$ is constant. The risky asset price A satisfies the stochastic differential equation

$$dA(t) = A(t)\gamma(Y(t))dt + A(t)\omega dB^1(t), A(0) = a > 0, \quad (2)$$

Where $\gamma : \square \to \square$ satisfies $(\gamma(y) - q)/\omega = y \; for \; y \in \square$. Then (2) can be written by

$$dA(t) = A(t)(q + \omega Y(t))dt + A(t)\omega dB^1(t).$$

We consider the division between the riskless asset and the risky assets. Let $\square^2(t_0, t_1)$ be a set of $\square(t)$-progressively measurable processes $\sigma : \psi \times [t_0, t_1] \to \square$ such that

$$P(\int_{t_0}^{t_1} \sigma(t)^2 dt < \infty) = 1 \quad (3)$$

We call an element of $\square^2(t_0, t_1)$ a portfolio strategy. We regard $\sigma_i(t)$ as a fraction of the wealth invested in the risky asset at time t. The wealth process U^σ corresponding to $\sigma \in \square^2(0,T)$ is given by

$U^\sigma(0) = u_0 > 0$ and

$$\begin{aligned} dU(t) &= U(t)\left[\sigma(t)(\gamma(Y(t)) - q) + q\right]dt + U(t)\sigma(t)\omega dB^1(t) \\ &= U(t)\left[\sigma(t)\omega Y(t) + q\right]dt + U(t)\sigma(t)\omega dB^1(t). \end{aligned} \quad (4)$$

There is incompleteness in the sense that there are some random processes that are not replicated by the self-financing portfolio strategy σ. The investor maximizes the expected utility of his wealth at terminal date T. We assume that the investor has a power utility function with a relative risk aversion coefficient δ:

$$\max_{\sigma \in Q_\delta(0,T)} E\left[\frac{U^\sigma(T)^{1-\delta}}{1-\delta}\right]. \quad (5)$$

Here Q_δ denotes the set of admissible portfolio strategies defined as follows. A Stochastic process σ is said to be an admissible portfolio strategy on $[t_0, t_1]$ if

(a) $\sigma \in \square^2(t_0, t_1), when \;\; 0 < \delta < 1$

(b) For some function $\tilde{\sigma} : [0,T] \times \square \to \square$ satisfying the linear growth condition ,

$\sigma(t) = \tilde{\sigma}(t, Y(t)) on [t_0, t_1], when \, \delta > 1.$

The set of all admissible strategies on $[t_0, t_1]$ is denoted by $Q_\delta[t_0, t_1]$. The choice of our set of portfolio strategies seems to be restrictive.

Because of incompleteness there is no unique equivalent martingale measure, and we cannot apply the so-called martingale approach directly. It is thus common to apply the dynamic programming approach using Hamilton-Jacobi-Bellman equation. Let

$$K(t,u,y;\sigma) = E^{t,u,y}\left[\frac{U^\sigma(T)^{1-\delta}}{1-\delta}\right],$$

Here and in the sequel, we use the notation $E^{t,u,y}[.] = E[.|U(t) = u, Y(t) = y]$.

Let $S = [0,T) \times (0,\infty) \times \square$. We then define $\zeta : S \to \square$ by

$$\zeta(t,u,y) = \sup_{\sigma \in Q_\delta(t,T)} K(t,u,y;\sigma).$$

The function ζ is called a value function. The Hamilton-Jacobi-Bellman equation related to the problem (5) is

$$\sup_{\sigma\in\square} C^{\sigma}H(t,u,y)=0 \qquad (6)$$

With the boundary condition $H(T,u,y)=\frac{u^{1-\delta}}{1-\delta}$, (7)

Where $C^{\sigma}H(t,u,y)=H_t+u(\sigma\omega y+q)H_u+\alpha(\bar{Y}-y)H_y$

$$+\frac{1}{2}u^2\sigma^2\omega^2H_{uu}+\frac{1}{2}\omega^2{}_YH_{yy}+\omega_Yu\sigma\omega\beta H_{uy}.$$

It is well known from Kim and Omberg and others that the function H is separable and has the following form:

$$H(t,u,y)=\frac{u^{1-\delta}}{1-\delta}g(t,y), \qquad (8)$$

Where $g(t,y)=\exp\left\{p(t)+s(t)y+\frac{1}{2}r(t)y^2\right\}$

With the boundary conditions $p(T)=s(T)=r(T)=0.$

It follows from the first order condition for (6) that the candidate optimal portfolio strategy is given by

$$\sigma^*(t)=\frac{1}{\delta}\frac{Y(t)}{\omega}+\frac{1}{\delta}\frac{\beta\omega_Y}{\omega}(s(t)+r(t)Y(t)). \qquad (9)$$

Substituting this conjectured solution into the Hamilton-Jacobi-Bellman equation, we obtain the differential equation for $p(.), s(.), and\ r(.)$ as follows:

$$\dot{r}(t)=-\omega^2{}_Y\left(\frac{1-\delta}{\delta}\beta^2+1\right)r(t)^2-2\left(\frac{1-\delta}{\delta}\omega_Y\beta-\alpha\right)r(t)-\frac{1-\delta}{\delta} \qquad (10)$$

$$\dot{s}(t)=-\omega^2{}_Y\left(\frac{1-\delta}{\delta}\beta^2+1\right)s(t)r(t)-\left(\frac{1-\delta}{\delta}\omega_Y\beta-\alpha\right)s(t)-\alpha\bar{Y}r(t) \qquad (11)$$

$$\dot{p}(t)=-\frac{1}{2}\omega^2{}_Y\left(\frac{1-\delta}{\delta}\beta^2+1\right)s(t)^2-\frac{1}{2}\omega^2{}_Yr(t)-\alpha\bar{Y}s(t)-(1-\delta)q \qquad (12)$$

3. Example:

Figure (1) Time dependent effects of ACTH on cortisol and DHEA's production in FA primary cultures. Primary human FA cells were prepared as described under Materials and methods, and plated at a density of 2,00,000 cells per well in 24 well dishes. The day before experiments, cells were changed to 1% low serum medium overnight. Cells were treated with ACTH (10nM) for the indicated times followed by quantification of medium cortisol and DHEA's using EIA kits. Steroid data were normalized to protein per well and expressed as the fold change over basal conditions (untreated cells) for each time point. Results represent the mean ±S.E.M. of data from at least three independent experiments. Three wells were analyzed for individual treatment in each experiment. Statistics were calculated using one way Anova followed by Dunnett's test, comparing with baseline. *P<0.05; **P<0.01; ***P<0.001 [10-15] & [18].

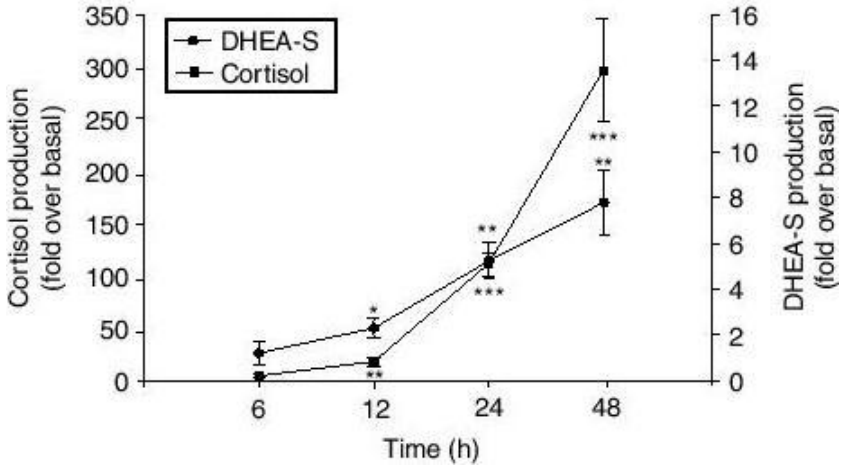

Figure (1): Effects of ACTH and DHEA's on cortisol production in human adult adrenal (AA) cells

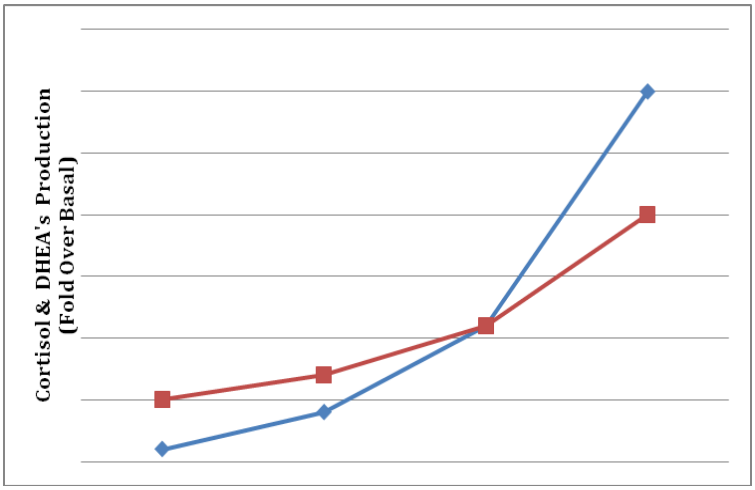

Figure (2): Effects of ACTH on cortisol and DHEA's production in human adult adrenal (AA) cells using Normal Distribution

4. Conclusion:

By applying a bio mathematical approach, we defined and estimate the genomic effects of ACTH in human adult and FA primary cultures. The newly defined adrenal ACTH responsive genes can provide clues to the mechanism of ACTH regulated steroidogenesis and cell growth, and may lead to further understanding of the global functions of ACTH in the adrenal gland. HJB equation with normal distribution gives the same as the medical report. The medical reports are beautifully fitted with the mathematical model. Hence the mathematical report {Figure (2)} is coincide with the medical report {Figure (1)}.

5. References:

1. Banerjee S, Dhar G, Haque I, Kambhampati S, Mehta S, Sengupta K, Tawfik O, Phillips T A & Banerjee S K, "CCN5/WISP-2 expression in breast adenocarcinoma is associated with less frequent progression of the disease and suppresses the invasive phenotypes of tumor cells", Cancer Research, Volume 68, Page Number 7606–7612, 2008.
2. Cecim M, Alvarez Sanz M, Van de Kar L, Milton S & Bartke A, "Increased plasma corticosterone levels in bovine growth hormone (bGH) transgenic mice: effects of ACTH, GH and IGF-I on in vitro adrenal corticosterone production", Transgenic Research, Volume 5, Page Number 187–192, 1996.
3. Gaillard I, Keramidas M, Liakos P, Vilgrain I, Feige J J & Vittet D, "ACTH-regulated expression of vascular endothelial growth factor in the adult bovine adrenal cortex: a possible role in the maintenance of the microvasculature", Journal of Cellular Physiology, Volume 185, Page Number 226–234, 2000.
4. Kim T S & Omberg E, "Dynamic nonmyopic portfolio behavior", The Review of Financial Studies, Volume 9, Page Number 141-161. 1996.
5. Korn R & Kraft H, "On the stability of continuous-time portfolio problems with stochastic opportunity set", Mathematical Finance, Volume 14, Page Number 403-413, 2004.
6. Le Roy C, Li J Y, Stocco D M, Langlois D & Saez J M, "Regulation by adrenocorticotropin (ACTH), angiotensin II, transforming growth factor-b, and insulin-like growth factor I of bovine adrenal cell steroidogenic capacity and expression of ACTH receptor, steroidogenic acute regulatory protein, cytochrome P450c17, and 3b-hydroxysteroid dehydrogenase", Endocrinology, Volume 141, Page Number 1599–1607, 2000.
7. Markowska A, Rebuffat P, Rocco S, Gottardo G, Mazzocchi G & Nussdorfer G G, "Evidence that an extrahypothalamic pituitary corticotrophin releasing hormone (CRH) adrenocorticotropin (ACTH) system controls adrenal growth and secretion in rats", Cell and Tissue Research, Volume 272, Page Number 439–445, 1993.
8. Merton R, "Life time portfolio selection under uncertainty: The continuous time case", Review of Economics and Statistics, Volume 51, Page Number 247-257, 1969.
9. Neri G, Andreis P G & Nussdorfer G G, "Comparison of ACTH and corticotrophin releasing hormone effects on rat adrenal steroidogenesis in vitro", Research in Experimental Medicine, Volume 191, Page Number 291–295, 1991.
10. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "A New Mathematical Model to Estimate the Effects of Lipid Induced Insulin Resistance on UPR mRNA Using Normal Distribution", International Journal for Research in Applied Science & Engineering Technology (IJRASET), Volume 3, Issue 9, Page Number 124-130, 2015.
11. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "A New Stochastic Model to Find the Insulin Secretion from Human Islets Using Exponential Distribution", IJRDO Journal of Mathematics, Volume 1, Issue 3, Page Number 72-79, 2015.

12. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "Stochastic Model to Estimate the Changes in Plasma Insulin and FFAs During OLTT and OGTT Using Normal Distribution", Bulletin of Mathematics and Statistics Research, Volume 3, Issue 3, Page Number 10-16, 2015.
13. Senthil Kumar P, Balasubramanian K & Dinesh Kumar A, "Stochastic Model to Estimate the Insulin Secretion Using Normal Distribution", Arya Bhatta Journal of Mathematics and Informatics (ABJMI), Volume 7, Issue 2, Page Number 277-282, 2015
14. Senthil Kumar P, Abirami R & Dinesh Kumar A, "Fuzzy Model for the Effect of rhIL6 Infusion on Growth Hormone", International Conference on Advances in Applied Probability, Graph Theory and Fuzzy Mathematics (ICAPGF), Proceedings Page Number 246-252, 2014.
15. Senthil Kumar P, Dinesh Kumar A & Vasuki M, "Stochastic Model to Find the Effect of Gallbladder Contraction Result Using Uniform Distribution", Arya Bhatta Journal of Mathematics and Informatics (ABJMI), Volume 6, Issue 2, Page Number 323-328, 2014.
16. Simmonds P J, Phillips I D, Poore K R, Coghill I D, Young I R & Canny B J, "The role of the pituitary gland and ACTH in the regulation of mRNAs encoding proteins essential for adrenal steroidogenesis in the late-gestation ovine fetus", Journal of Endocrinology, Volume 168, Page Number 475–485, 2001.
17. Toshiki Honda & Shoji Kamimura, "On the verification theorems of continuous time optimal portfolio problems with stochastic market price of risk", Citation, Volume 1443, Page Number 144-150, 2005.
18. Yewei Xing, Richard Parker C, Michael Edwards & William E Rainey, "ACTH is a potent regulator of gene expression in human adrenal cells", Journal of Molecular Endocrinology, Volume 45, Page Number 59–68, 2010.
19. "An intertemporal capital asset pricing model", Econometrica, Volume 41, Page Number 867-887. 1973.
20. "Optimum consumption and portfolio rules in a continuous time model", Journal of Economic Theory, Volume 3, Page Number 373-413, 1971.