Stochastic Modeling and Applications
Vol. 25 No. 1 (January-June, 2021)

Received: 06th March 2021 *Revised: 13th April 2021* *Selected: 20th June 2021*

A MATHEMATICAL MODEL FOR HYPOTHALAMIC - PITUITARY - ADRENAL AXIS RESPONDS DIFFERENTLY TO MORNING AND EVENING PSYCHOLOGICAL STRESS IN HEALTHY PEOPLE USING GENERALIZED CAUCHY FAMILY OF DISTRIBUTIONS

A. MANICKAM AND A. LEEMA ROSE

Abstract. The study's goal is to see if the timing of day has an influence on the acute response of the HPA axis activity to acute stressors using a Cauchy distribution. The hypothalamic-pituitary-adrenal (HPA) axis reacts to environmental factors, particularly psychological stresses. The TSST measures the daytime cycle of salivary cortisol as well as the stress reaction of salivary cortisol and heart rate. Finally, we determine that the implementation portion corresponds to a mathematical model, and the outcome is connected to the medical report. This study will be very useful in the medical career in the future.

1. Introduction

The Cauchy distribution, named after Augustin Cauchy, is a simple family of distributions for which there is no estimated value. Furthermore, the family is closed under the construction of sums of random variables, indicating that it is an endlessly divisible family of distributions. [19, 21, 27] utilized the Cauchy distribution to produce an explicit equation for $P\left(Z_1 \leq 0, Z_2 \leq 0\right)$, where $\left(Z_1, Z_2\right)^T$ follows the typical bivariate normal distribution. The Cauchy distribution has been employed in a variety of applications, including electrical and mechanical theory, physical anthropology, assessment difficulties, activities and financial research.

It was used to simulate the impact sites of a fixed single direction of particles released from a measurement device [5, 10, 11]. It is known as a Lorenzian distribution in physics, and that is the distribution [15, 16, 17, 18] of the power of an unstable state in quantum theory.

2. Mathematical model and Assumptions

The random variable X in $T-R\{Y\}$ family of distributions is defined as

$$F_X\left(x\right) = \int_a^{Q_Y\left(F_R(x)\right)} f_T(t)dt = F_T\left(Q_Y\left(F_R\left(x\right)\right)\right) \tag{2.1}$$

2000 *Mathematics Subject Classification.* $62H_{xx}$, $62NO_5$, 90B25.

Key words and phrases. HPA axis, Salivary Cortisol, Cauchy distribution, Hazard function.

The corresponding PDF associated with (2.1) is

$$f_X(x) = f_T(Q_Y(F_R(x))) \times Q^1{}_Y(F_R(x)) \times f_R(x) \tag{2.2}$$

Alternatively, (2.2) can be written as

$$f_X(x) = f_R(x) \times \frac{f_T(Q_Y(F_R(x)))}{f_Y(Q_Y(F_R(x)))} \tag{2.3}$$

The hazard function of the random variable X can be written as

$$h_X(x) = h_R(x) \times \frac{h_T(Q_Y(F_R(x)))}{h_Y(Q_Y(F_R(x)))} \tag{2.4}$$

[2, 3, 4] studied, respectively, the T-R{exponential}, T-normal{Y} and T-gamma{Y} families of distributions. [1, 20, 22, 23] studied some general properties of the T-R{Y} family. Now, we define the T-Cauchy{Y} family.

Let R be a random variable that follows the Cauchy distribution with PDF

$$F_R(x) = F_C(x) = \pi^{-1}\theta^{-1}(1 + x/\theta^2)^{-1} \text{ and CDF}$$
$$F_R(x) = F_C(x) = 0.5 + \pi^{-1}\tan^{-1}(x/\theta\ ), x \in R, \theta > 0,$$

then (2.3) reduces to

$$f_X(x) = f_C(x) \times \frac{f_T(Q_Y(F_C(x)))}{f_Y(Q_Y(F_C(x)))} \tag{2.5}$$

Hereafter, the family of distributions in (2.5) will be called the T-Cauchy{Y} family. It is clear that the PDF in (2.5) is a generalization of Cauchy distribution.

3. Applications

The hypothalamic-pituitary-adrenal (HPA) axis and sympatho adrenal medullary (SAM) system are important in response to stress. To begin with, the SAM system responds swiftly to stress, causing an elevated heart rate. Secondary, the HPA axis responds more slowly by secreting glucocorticoid hormones such as corticosterone in rats and cortisol in humans. Cortisol is the major stress response in humans, acting as an indicator of HPA axis function in response to stress. The cortisol reaction to intense stressors is regulated by the participants age [9, 14] gender [6, **?**] and mood conditions [8, 25]. In terms of the influence of rest on cortisol levels, both full and partial sleep loss raise the basal level of HAP axis activity [15, **?**]. Shorter sleep duration and poor sleep efficiency have also been linked to a greater response to acute mental stress [26].

In this work, we looked at how the HPA axis responds to stressful events in the morning and evening using TSST in healthy people. The TSST timings were chosen based on personal variations in the circadian rhythms of cortisol levels and the sleep wake cycle. Because recurrent TSST causes a significant degree of conditioning of the HPA axis reaction, the participants only conducted TSST once, whether in the morning or in the evening [7, 13].

Figure 1 depicts the average diurnal rhythm of salivary cortisol in the baseline condition. Panelists A diurnal cycle of salivary cortisol level assessed on the last day of baseline condition was shown.

Figure 2 Salivary cortisol responses in the morning and evening before and after the Trier Social Stress Test (TSST). Panel A depicts the average salivary insulin levels pre and post TSST in the morning and evening. Horizontal bars with open and closed ends represent 5 minute anticipation and 10 minute TSST intervals, respectively.In normal young volunteers, we were able to establish that the transient stress reaction to the HPA axis elicited by the TSST had a substantial time of day variation (morning vs evening).

The HPA axis activity shows a stronger reaction to acute mental stress in the morning rather than the evening (Figure 2), although the sympathoadrenal medulla system did not exhibit a substantial time of day difference was observed in terms of rise in HR (Figure 3). Pulse rate reactions in the morning and evening during the Trier Social Stress Test (TSST).

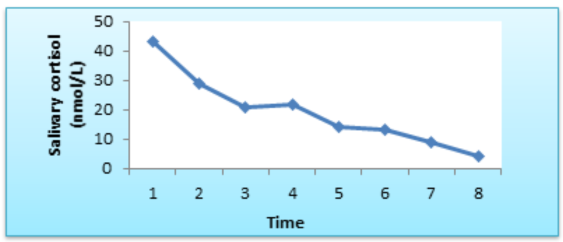

FIGURE 1.

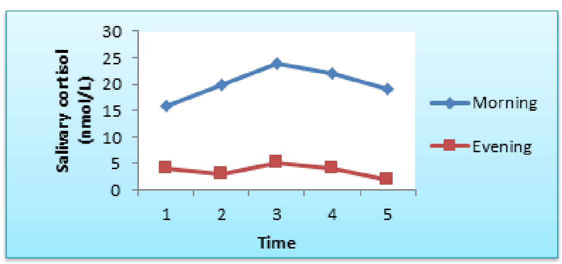

FIGURE 2.

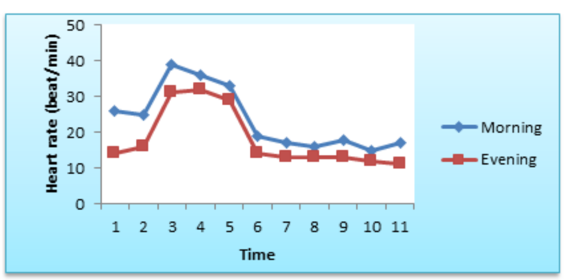

FIGURE 3.

In conclusion, we were able to show that the HPA axis activity reaction to severe stressors is greater in the morning than in the evening, which correlates with the circadian rhythm of cortisol concentration. When assessing individual HPA axis activity reactions to diverse stresses, it is critical to take into account the patient's circadian rhythm and period of day.

4. Mathematical Results

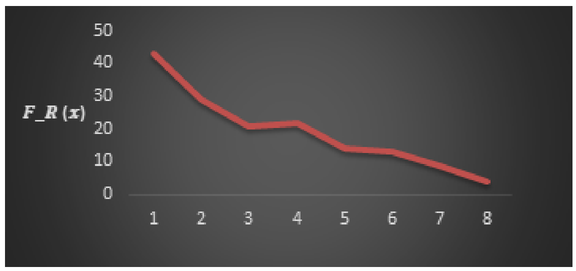

FIGURE 4.

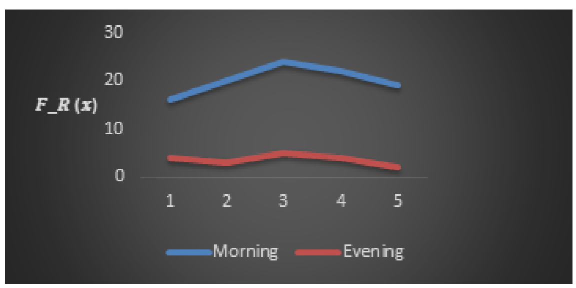

FIGURE 5.

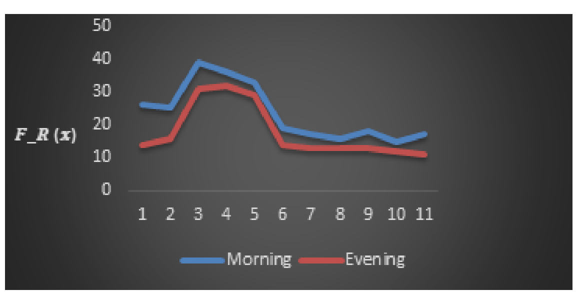

FIGURE 6.

5. Conclusion

The HPA reaction to chronic mental stress was stronger in the morning than in the evening, consistent with the diurnal control of cortisol production. We displayed probability density function, cumulative function, and hazard function for collected health data. It is thought that the extension of the Cauchy distribution model is well suited for mathematical analysis of health records. It is beneficial to healthcare workers.

Acknowledgements

The authors would like to thank the National Institute of Medical Science, IISC Bangalore for the use of ANSYS software.

Conflict of Interests

The authors declare that there is no conflict of interests.

References

1. Aljarrah, M.A., Lee, C., Famoye, F., On generating T-X family of distributions using quantile functions. *J. Stat. Distrib. Appl.* 1 (2014) 1 –17.
2. Alzaatreh, A., Lee, C., Famoye, F., A new method for generating families of continuous distributions. *Metron* 71(1) (2013) 63–79.
3. Alzaatreh, A., Lee, C., Famoye, F., T-normal family of distributions: a new approach to generalize the normal distribution. *J. Stat. Distrib. Appl.* 1 (2014) 1 –16.
4. Alzaatreh, A., Lee, C., Famoye, F., Family of generalized gamma distributions: properties and applications. To appear in Hacettepe *Journal of Mathematics and Statistics.* (2015).
5. Appalanaidu ,V., Manickam ,A., A Mathematical model for suppression of growth hormone - dependent isoforms of cytochrome P450 in female rats by the somatostain analog octreotide. *IOSR Journal of Mathematics* (IOSR-JM) e-ISSN: 2278-5728, p-ISSN: 2319-765X. 13(4) Ver. III (2017) 01-04.
6. Eisenberger ,N.I., Taylor ,S.E., Gable ,S.L., Hilmert ,C.J., Lieberman ,M.D., Neural pathways link social support to attenuated neuroendocrine stress responses. Neuro Image. 35(4) (2007) 1601–12.
7. Goodman ,W.K., Janson ,J., Wolf ,J.M., Meta-analytical assessment of the effects of protocol variations on cortisol responses to the Trier Social Stress Test. Psychoneuroendocrinology. 80 (2017) 26–35.
8. Het ,S., Wolf ,O.T., Mood changes in response to psychosocial stress in healthy young women: effects of pre treatment with cortisol. *Behav Neurosci.* 121(1) (2007) 11–20.
9. Hidalgo, V., Pulopulos ,M.M., Puig-Perez, S., Espin,L., Gomez-Amor , J., Salvador ,A ., Acute stress affects free recall and recognition of pictures differently depending on age and sex. *Behav Brain Res.* 292 (2015) 393–402.
10. Kalaiselvi ,R., Manickam ,A., Mamta Agrawal and Pushpendrakumar., A study of mathematical model for Extended Lognormal Distribution to obligatory Role of Hypothalamic Ovariectomized Rhysus Monkey, *Annals of the Romanian society for cell Biology:* ISSN: 1583-6258, 25 (5) 4122-4127.
11. Kalaiselvi .R, Manickam,A and Mamta Agrawal., A mathematical model for maximum Likelihood Estimation to Atrazine Inhibits pulsatile Gonatropin-Releasing Hormone in Animals, *Turkish Journal of Computer and Mathematics Education:* ISSN: 1309-4653 12(3) (2021) 3550-3554.
12. Kirschbaum ,C., Pirke ,K.M., Hellhammer ,D.H., The 'Trier Social Stress Test' – a tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology.* 28(1–2) (1993)76–81.

13. Kudielka , B.M., Buske-Kirschbaum ,A., Hellhammer, D.H., Kirschbaum ,C., HPA axis responses to laboratory psychosocial stress in healthy elderly adults, younger adults, and children: impact of age and gender. *Psychoneuroendocrinology.*29(1) (2004) 83–98.
14. Leproult ,R., Copinschi ,G., Buxton ,O., Van Cauter ,E., Sleep loss results in an elevation of cortisol levels the next evening. Sleep. 20 (10) (1997) 865–70.
15. Manickam , A., A Mathematical Model for Analysis of Progonostification of Nasopharyal Carcinoma, Advances in Mathematics: *Scientific Journal* 8(3) (2019) 673–676 *(Special issue on ICRAPAM)* ISSN 1857-8365(p) ISSN 1857-8438(e)
16. Manickam , A., The Steady state and the Transient behavior ofthe model to predict the tolerance level when the administration of PEGGHRH and GHRH in human, *International Journal of Engineering, Science and Mathematics*, 7 (5) (2018) 193-206, ISSN: 2320-0294.
17. Manickam , A., A Bivariate Exponential distribution model for growth hormone response to repeated maximal cycle ergometer exercise at different pedaling rates.*International Journal of Engineering Research and Application*, ISSN: 2248-9622, 7(11), Part - 3 (2017) 28-33.
18. Manickam , A., A Mathematical model using for the fluvoxamine reduces responsiveness of hpa axis in adult female bpd patients with a history of sustained childhood abuse, *International Journal Of Advancement In Engineering Technology, Management and Applied Science (IJAETMAS)* (Number-63082). ISSN: 2349-3224 , 05(07) (2018).
19. Manickam , A., A Study On Weibull-G Exponential Distribution Model For Secretion Of Gnrh In Beef Cows *Advances in Mathematics: Scientific Journal*, 8(9) (2020) 7477–7482 ISSN 1857-8365 printed version ISSN 1857-8438 electronic version(SCOPUS INDEXED)UGC APPROVED JOURNAL Sep 2020.
20. Manickam , A., A Mathematical Extended reliability growth model for the measurement of GH, Insulin-like growth factor-1 and the aging cardio vascular system. *International Journal of Applied Mathematics and Statistics* e-ISSN: 0973-7545, p-ISSN: 0973-1377. 56(6) (2017) 73-78.
21. Manickam ,A., A Bivariate Exponential Distribution Model For Dependent Feedback Inhibition Of Pulsatile Growth Hormone Secretion. *International Journal Of Research and Analytical Reviews.(IJRAR)*. ISSN: 2349-5138, 06(01) (2019).
22. Manickam ,A., A Mathematical Model for Regulation of Fuel Metabolism during Exercise in Hypopituitarism with Growth Hormone Deficiency , *International Journal of Applied Engineering Research.* ISSN 0973-4562, 12(21) (2017) 11330-11335.
23. Manickam ,A., A Mathematical Model For Pulsatile Gonadotropin-Releasing Hormone Release From Hypothalamic Explants Of Male Marmoset Monkeys Compared With Male Rats, *Advances in Mathematics: Scientific Journal*, 10(1) (2021) 629-636.
24. Melhem ,N.M., Keilp ,J.G., Porta ,G et al., Blunted HPA axis activity in suicide attempters compared to those at high risk for suicidal behavior. *Neuropsycho pharmacology*, 41(6) (2016) 1447–56.
25. Raikkonen,K., Matthews,K.A., Pesonen,A.K., et al. Poor sleep and altered hypothalamic-pituitary-adrenocortical and sympatho-adrenalmedullary system activity in children. *J Clin Endocrinol Metab*, 95(5) (2010) 2254–61.
26. Uhart,M., Chong ,R.Y.,Oswald ,L., Lin,P.I., Wand,G.S., Gender differences in hypothalamic-pituitary-adrenal (HPA) axis reactivity. *Psycho neuroendocrinology.* 31(5) (2006) 642–52.
27. Wright ,K.P Jr., Drake ,A.L., Frey , et al. Influence of sleep deprivation and circadian misalignment on cortisol, inflammatory markers, and cytokine balance. *Brain Behav Immun.* 47 (2015) 24–34.

A. Manickam : Research Advisor, Department of Mathematics, Marudupandiyar college(Arts & Science), (Affiliated to Bharathidasan University, Tiruchirappalli-620 024), Thanjavur-613 403, Tamil Nadu, India
Email address: manickammaths2011@gmail.com

A. Leema Rose : Research Scholar, Department of Mathematics, Marudupandiyar college(Arts & Science), (Affiliated to Bharathidasan University, Tiruchirappalli-620 024), Thanjavur-613 403, Tamil Nadu, India
Email address: anto.leema14@gmail.com