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A MULTI-VARIATE MODEL FOR THE COMBINED PROPRANOLOL / TSST PARADIGM

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ABSTRACT:

The sampling distribution of many (multivariate) statistics are normal, regardless of the parent distribution (Multivariate central limit theorems). Thus, for large sample sizes, we may be able to make use of results from the multivariate normal distribution to answer our statistical questions, even when the parent distribution is not multivariate normal. The mathematical results have been obtained by using bivariate normal distribution for the combined propranolol/TSST Paradigm and with the comparison of three cases namely cortisol and stress; amylase and heart rate; systolic and diastolic blood pressures. These are all well explained in mathematical figures of section 3.

Keywords: ***Cortisol, CRH, ACTH, Propranolol, Stress.***

2010 AMS Classification: 62HXX, 60EXX

1. MATHEMATICAL MODEL

Applied problems are so complex that it would only be interesting from a mathematical perspective. It is mathematically tractable for a larger number of problems, and therefore, progress towards answers to statistical questions can be provided, even if only approximately so. Because it is tractable for so many problems, it provides insight into techniques based upon other distributions or even non-parametric techniques. For this, it is often a benchmark against which other methods are judged. For some problems it serves as a reasonable model of the data. In other instances, transformations can be applied to the set of responses to have the set conform well to multivariate normality. The sampling distribution of many (multivariate) statistics are normal, regardless of the parent distribution (Multivariate Central Limit Theorems). Thus, for large sample sizes, we may be able to make use of results from the multivariate normal distribution to answer our statistical questions, even when the parent distribution is not multivariate normal [5, 6, 8, 10, 11, 12].

Consider first the univariate normal distribution with parameters μ (mean) and σ (variance) for the random variable x,

$$f(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{\frac{-1}{2}\frac{(x-\mu)^2}{\sigma^2}} \qquad (1.1)$$

For $-\infty < x < \infty, -\infty < \mu < \infty, and\ \sigma^2 > 0.$

Now rewrite the exponent $(x-\mu)^2/\sigma^2$ using the linear algebra formulation of

$(x-\mu)'(\sigma^2)^{-1}(x-\mu)$.

This formulation matches that for the generalized or Mahalanobis squared distance $(x-\mu)'\sum^{-1}(x-\mu)$, where both x and μ are vectors. The multivariate normal distribution can be derived by substituting the Mahalanobis squared distance formula into the univariate formula and normalizing the distribution such that the total probability of the distribution is 1. This yields,

$$f(x) = \frac{1}{(2\pi)^{p/2}|\sum|^{1/2}} e^{\frac{-1}{2}(x-\mu)'\sum^{-1}(x-\mu)} . \qquad (1.2)$$

for $-\infty < x < \infty, -\infty < \mu < \infty,$ and for $\sum$ positive definite.

In the bivariate normal case the squared distance formula, in terms of the individual means μ_1 and $\mu_{2,}$ variances σ_{11} and $\sigma_{22,}$ and correlation $\rho_{12,}$ is

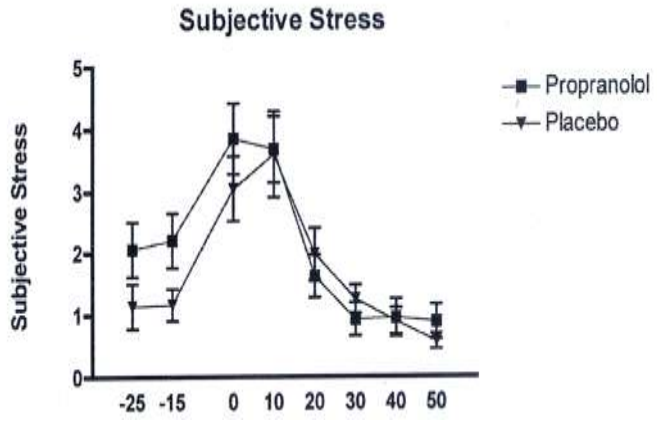
$$(x-\mu)'\sum^{-1}(x-\mu) = \frac{1}{1-\rho_{12}^2}\left[\left(\frac{x_1-\mu_1}{\sqrt{\sigma_{11}}}\right)^2 + \left(\frac{x_2-\mu_2}{\sqrt{\sigma_{22}}}\right)^2 - 2\rho_{12}\left(\frac{x_1-\mu_1}{\sqrt{\sigma_{11}}}\right)\left(\frac{x_2-\mu_2}{\sqrt{\sigma_{22}}}\right)\right] \qquad (1.3)$$

2. APPLICATION:

In the current study, we aim to investigate that the interaction between the SNS (Sympathetic Nervous System), HPA (Hypothalamic Pituitary Axis) and the subjective emotional stress experience during a psychological stress task. The significant decrease in heart rate and SAA (Salivary Alpha Amylase) levels in the **Propranolol** group confirms the effectiveness of the pharmacological procedure [3,4]. However, no significant differences between the groups for the diastolic blood pressure measurements were observed, together with a strong trend for systolic blood pressure. Also, increased cortisol levels were observed in the **Propranolol** group. The increased cortisol in the **Propranolol** group may have significant implication for the use of propranolol as a treatment for cardiovascular disease and/or social anxiety in the long term [10]. In subjective stress, there is a overall depicting a response pattern of stress perception peaking immediately pre and post Trial Social Stress Test [2]. The analysis of the salivary alpha amylase revealed a significant interaction effect of time by group.

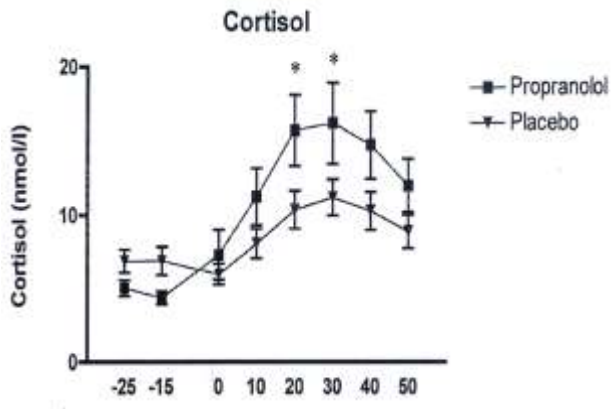
The overall heart rate results confirm the suppressing effect of propranolol on the SNS, where all samples in the propranolol group were found to be significantly lower compared to the placebo group. The **Anova's** with the systolic and diastolic blood pressure levels as dependent variables did not reveal a significant interaction effect of time or main effect of group for either variable group.

In conclusion, the combined **Propranolol**/TSST paradigm allows to investigate the interaction between the SNS, HPA and subjective experiences during acute stress. The results suggest an inverse relationship between the SNS and HPA, where suppression of the SNS leads to an inverse of activity of HPA [1]. Finally, the **Propranolol**/TSST paradigm could be especially useful when aiming to detect possible dysregulations of the HPA axis in response to psychological stress, since the use of **Propranolol** amplifies the HPA axis response to psychosocial stress.



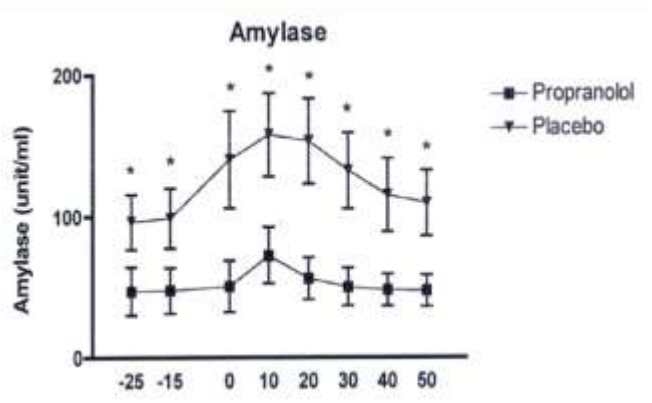
Effects of the TSST on subjective stress ratings in relation to the two experimental propranolol propranolol (n=15) conditions: propranolol (n=15) and placebo (n=15).

Figure2.1



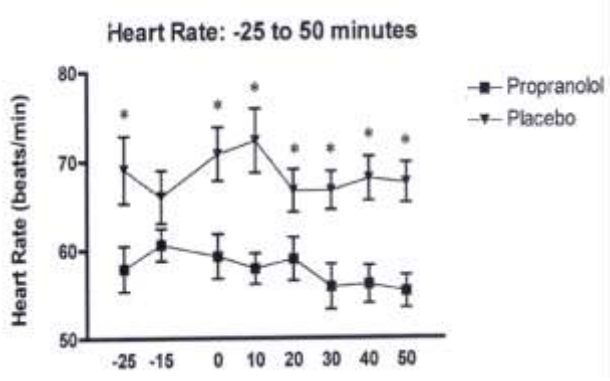
Effects of the TSST on the cortisol response in relation to the two experimental conditions and placebo (n=15).

Figure2.2



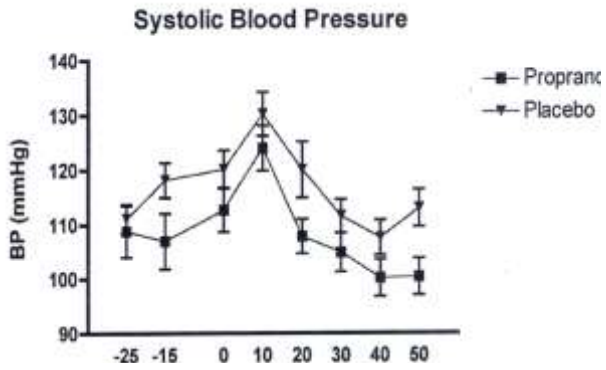
Effects of the TSST on the salivary alpha-amylase response in relation to the two experimental propranolol(n=15) and placebo(n=15)

Figure2.3



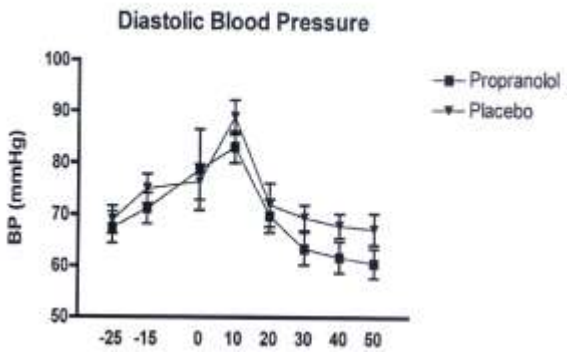
Effects of the TSST on the heart rate in relation to the two experimental conditions: propranolol(n=15) and placebo(n=15)

Figure2.4



Effects of the TSST on the systolic blood pressure in relation to the two experimental conditions:propranolol (n=15) and placebo (n=15).

Figure2.5



Effects of the TSST on the diastolic blood pressure in relation to the two experimental conditions: propranolol(n=15) and placebo (n=15).

Figure2.6

3. MATHEMATICAL RESULTS

By using bivariate normal distributions from equation (1.3) we get the following figures.

(i) For cortisol and stress.

(ii) For amylase and heart rate.

(iii) For systolic and diastolic blood pressures.

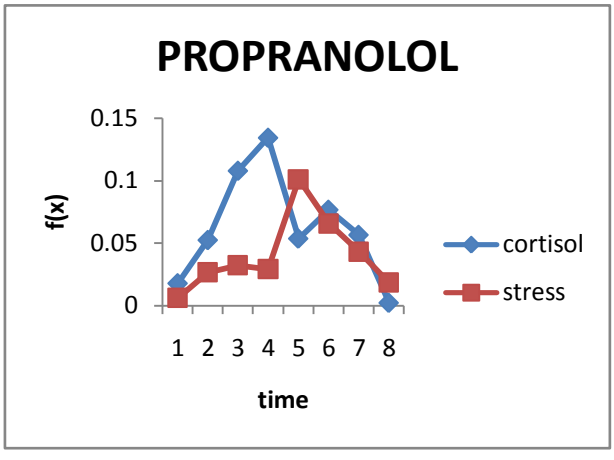


Fig3.1

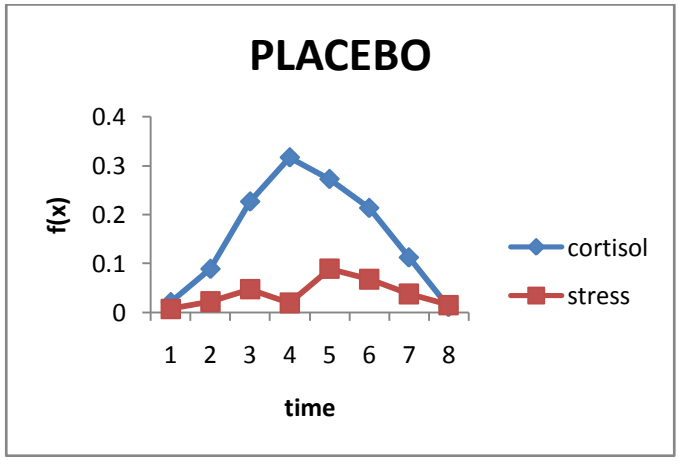


Fig3.2

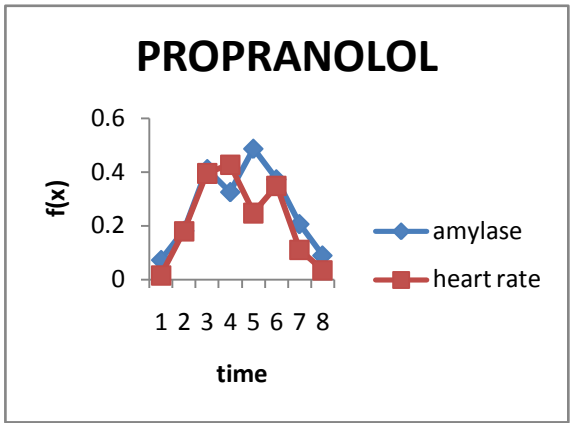


Fig3.3

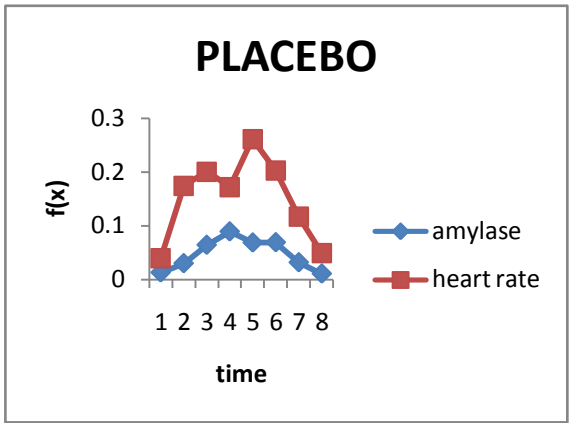


Fig3.4

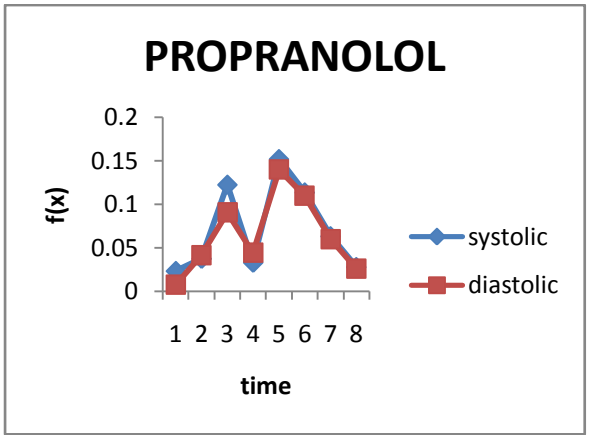


Fig3.5

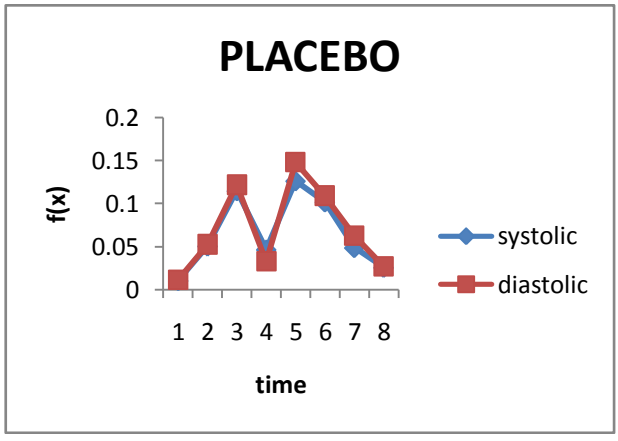


Fig3.6

4. CONCLUSION

The mathematical results have been obtained by using bivariate normal distribution for the combined propranolol/TSST Paradigm and with the comparison of three cases namely, when the stress value is 0.1, the corresponding cortisol value is 0.14 in the propranolol case and 0.3 in placebo case. When the heart rate is 0.5, the corresponding amylase value is 0.45 in propranolol case and when the heart rate is 0.28, the corresponding amylase 0.1 in the placebo case. In Fig (3.5), both systolic and diastolic pressures reach the same value 0.15 in the propranolol case. When the value of systolic pressure is 0.13, the corresponding diastolic pressure is 0.15 in the placebo case.

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