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Effects of Dopamine Receptors in Drugs Under Transient State and Steady State

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***Abstract*—This paper deals with a neurotransmitter called Dopamine. Lack of Dopamine causes mental disorders. We analyze some medicines to increase Dopamine and find the most safe and effective medicine with less side effects by means of Transient State and Steady State. We graphically represent the performance measure values and find the best medicine.**

***Index Terms*—Dopamine Receptors, various medicines, Transient state, Steady state.**

I. Introduction

In Brain, we have many neurotransmitters, which is responsible for transmit- ting signals in between the nerve cells. Here, we analyse a neurotransmitter called Dopamine receptor, which is made of very few neurons. Dopamine works for improving the heart's pumping strength and the blood flow to the kidneys. Dopamine is a chemical messenger in the brain, which is in- volved in reward, motivation memory, attention and even regulating body movements. Dopamine injection is given in condition when we are in shock, which is caused by heart attack kidney failure, surgery, trauma and several medical conditions.

Shitij Kapur, John Mann studied on the 'Role of the dopaminergic sys- tem in depression'. Abhinav Anand [2010], proposed a 'Queuing Theory Model for Insulin Level and Number of Insulin Receptors in Body'. Also, Ca- gin Kandemir-Cavas, Levent Cavas [2007], derive, 'An application of Queu- ing Theory to the Relationship between Insulin Level and Number of Insulin Receptors'.

Destexhe A, ZF Mainen, Sejnowski TJ [1994] estimated, 'An efficient method for computing synaptic conductances based on a kinetic model of receptor finding'. Abbasi NA, Akan OB [2015], studied 'A queuing theoreti- cal delay analysis for intrabody nervous nanonetwork'. Wysocki BJ, Martin TM [2013], discussed an, 'Modelling non-viral gene delivery as a macro-to- nano communication system'.

In Dopamine receptor, we have five subtypes, listed from D1 to D5. Each function as metabotropic, G protein-coupled receptors. It is again subdivided into two families, as D1-like receptor and D2-like receptor.

From the Table-1, D1-like receptor consists of two G protein coupled receptor that are coupled to G5 and mediate excitatory neurotransmission which include D1 and D5. D2-like receptor consists of three G-protein cou- pled receptor that are coupled to G_i / G_o and mediate inhibitory neurotrans- mission which include D2, D3 and D4.

D1 receptors are the most numerous dopamine receptors in human nervous system, D2 receptors are next; D3, D4 and D5 receptors are present at significantly lower levels.

A. Drugs to Increase Dopamine Level in Brain

Many mental disorders such as Schiyopherenia, Parkinson's disease, bipo- lar disorder acute prychris, hallucinations etc., make human brain to drop the dopamine level. Thus, the patients with low level of dopamine level take some drug either by mouth or by injection into muscles, will increase the level of dopamine so that they behave normally. Some of the drugs which are commonly used is, Haloperidol, Spiperone, Risperidone, Thioridazine, and Chlorpromazine.

We now find the best drug from the reaction of dopamine in the drug by normal and increasing the level of dopamine in the drug, using the multi- server heterogeneous model M/M/3. Also, we find this in transient state and steady with graphical representation.

TABLE I
Family, Receptor, Gene, Type and Mechanism

Family	Receptor	Gene	Type	Mechanism
D1-like	D1 D5	DRD1 DRD5	G_s -coupled	Increase intracellular levels of CAMP by activating adenylate cyclase
D2-like	D2 D3 D4	DRD2 DRD4 DRD4	G_i -coupled	Decrease intracellular levels of CAMP by inhibiting adenylate cyclase

TABLE II
TRANSIENT STATE PROBABILITIES FOR DRUGS

	Haloperidol	Spiperone	Risperidone	Thioridazine	Chlorpromazine
$P_0(0.1)$	0.4199587	0.586574252	0.382084907	0.358140799	0.64047598
$P_1(0.1)$	0.412152782	0.438184255	0.45997892	0.4628745	0.42824761
$P_2(0.1)$	0.150270521	0.167283774	0.122413435	0.23814353	0.148384353
$P_3(0.1)$	0.19478988	0.04088461	0.030920939	0.02084039	0.045183614
$P_4(0.1)$	0.011120098	0.010141353	0.0065406419	0.00546190	0.012183641
$P_5(0.1)$	0.0086743213	0.0039637157	0.010369038	0.00328924	0.008146236
$P_6(0.1)$	0.0073592890	0.001986992	0.008885341	0.000126428	0.002418543

TABLE III
L_S, L_Q, W_S AND W_Q VALUES USING TRANSIENT PROBABILITY

Drugs	L_s	W_s	L_q	W_q
Haloperidol	0.67127907	0.279699612	0.040546607	0.021061086
Spiperone	0.704259528	0.230648822	0.024029762	0.060074406
Risperidone	0.744678868	0.310282862	0.053838947	0.082432894
Thioridazine	0.626096068	0.141964742	0.062419604	0.0022999377
Chlorpromazine	0.601041661	0.176776959	0.035731742	0.010509335

II. TRANSIENT STATE

A transient state is a state in which variables change over time. By applying Runge-kutta IV order method, a family of implicit and explicit iterative method, which includes the well-known routine called the Euler Method, used in temporal discretization for the approximate solutions of ordinary differential equations. These methods were developed around 1900 by the German mathematicians C.Runge and M.W. Kutta.

We calculate and tabulate the values using the M/M/3 formula as,

$$P_n = \left(\frac{1}{n}\left(\frac{\lambda}{\mu}\right)^n\right) P_0 \quad (1)$$

$$P_0 = \left[\sum_{n=0}^{c-1} \frac{\rho^n}{n!} + \frac{\rho^c}{c!}\left(\frac{1}{1-\frac{\rho}{c}}\right)\right]^{-1} \quad (2)$$

Using the above formula we calculate the values of P_0 (0.1),P1(0.1).....P6(0.1) as

From the above tabulated values we find,

L_s - Average level of dopamine in the drug

W_s - Waiting time for reaction of drug in patient

L_q - Average level of increase of dopamine in the drug.

W_q - Waiting time for reaction of patient while increase of dopamine in drug. Using the multi-server queuing model M/M/3 formula,

$$L_q = \sum_{n=c}^{\infty}(n - c)\, P_n \quad (3)$$

$$W_q = \frac{L_q}{\lambda} \quad (4)$$

$$W_s = W_q + \frac{1}{\mu} \quad (5)$$

$$L_q = \lambda W_s \quad (6)$$

With the help of the values available in Table-2, and using the above formulas L_q, W_q, W_s and L_s values are evaluated and tabulated. The tabulated values are presented in the graph.

In Fig. 1, x-axis represents the different types of drugs and y-axis represents, average level of dopamine in the drug.

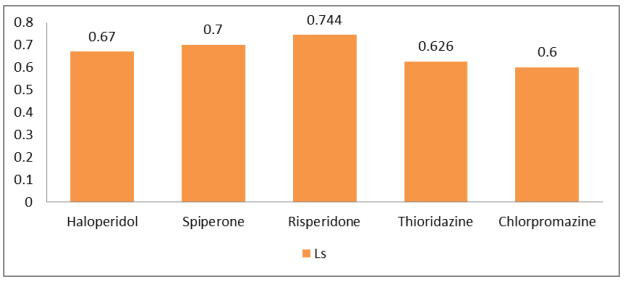

Fig. 1. Average level of dopamine in the drug

The Fig. 1, exhibits, the level of dopamine in the drug. In which, level of dopamine is high in Risperidone. Spiperone is the second highest drug. Thioridazine is the drug with least level of dopamine.

In Fig. 2, x-axis represents the different types of drugs and y-axis represents, waiting time for reaction of drug in patient.

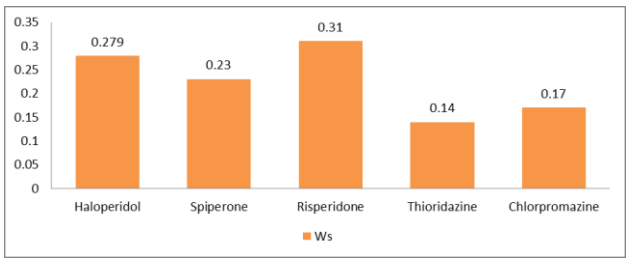

Fig. 2. Average waiting time for reaction of drug in patient

The Fig. 2, represents, the average waiting time for reaction of drug in patient. In which, level of dopamine is high in Risperidone. Haloperidol is the second highest drug.

Thioridazine is the drug with least level of dopamine.

Hence, by comparing both the Fig.1 and Fig. 2, more the level of dopamine in the drug, the more the reaction of drug in patients. From this we conclude that, the drug Risperidone is the most safe and effective medicine to the patients and Thioridazine is the drug with more side effects and so it should not be used.

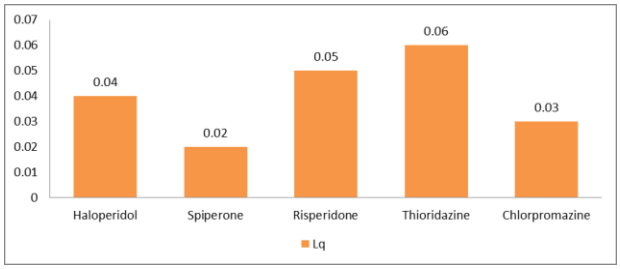

Fig. 3. Average level of increase of dopamine in the drug

The Fig. 3, displays, the increase in level of dopamine in the drug, where the x-axis represents the different types of drugs and y-axis represents, average level of increase of dopamine in the drug. In which, level of dopamine is high in Thioridazine. Risperidone is the second highest drug. Spiperone is the drug with least level of dopamine.

In Fig. 4, x-axis represents the different types of drugs and y-axis represents, Waiting time for reaction of patient while increase of dopamine in drug.

The Fig. 4, protrays, waiting time for the reaction of patients after increasing the level of dopamine in the drug. In which, level of dopamine is high in Risperidone. Spiperone is the second highest drug. Thioridazine is the drug with least level of dopamine.

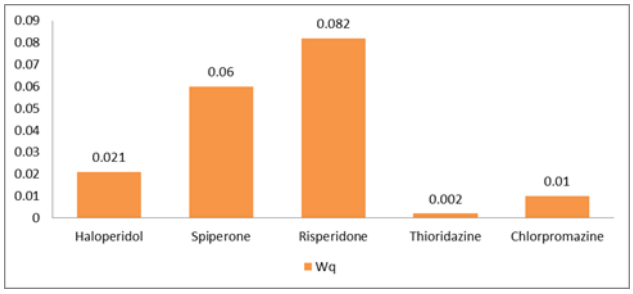

Fig. 4. Average waiting time for reaction of patient while increase of dopamine in drug

Thus, from Fig. 3 and Fig. 4, we notice that, even if the level of dopamine is higher in the Thioridazine drug, it has the most least reaction in patients.From this we terminate that, the Thioridazine is not safe and effective drug to use because of its side effects. Therefore it should not be prescribed.

III. Steady State

A state or condition of a system or process that does not change in time is called as Steady State. We now calculate some important performance measures independent of time such as,

L_s- Average level of dopamine in the drug

W_s- Waiting time for reaction of drug in patient

L_q- Average level of increase of dopamine in the drug.

W_q- Waiting time for reaction of patient while increase of dopamine in drug. By using the formulas,

$$L_s = \frac{\lambda\mu(\lambda/\mu)^c P_0}{(c-1)!(c\mu-\lambda)^2} + \frac{\lambda}{\mu} \quad (7)$$

$$W_s = \frac{\lambda\mu(\lambda/\mu)^c P_0}{(c-1)!(c\mu-\lambda)^2} \quad (8)$$

$$L_q = \frac{\mu(\lambda/\mu)^c P_0}{(c-1)!(c\mu-\lambda)^2} \quad (9)$$

$$W_s = \frac{\mu(\lambda/\mu)^c P_0}{(c-1)!(c\mu-\lambda)^2} + \frac{1}{\mu} \quad (10)$$

The following table shows the calculated values of L_q, L_s, W_s and W_q using above formulas,

With the help of graphical representation we examine which drug has more dopamine level in drug and which drug reacts the most in patient by com- paring L_s and W_s values from the Table-4. In Fig. 5, x-axis represents the different types of drugs and y-axis represents, the average level of dopamine in the drug.

The Fig. 5 exhibits, the level of dopamine in the drug.In which, level of dopamine is high in Risperidone. Thioridazine is the second highest drug. Spiperone is the drug with least level of dopamine.

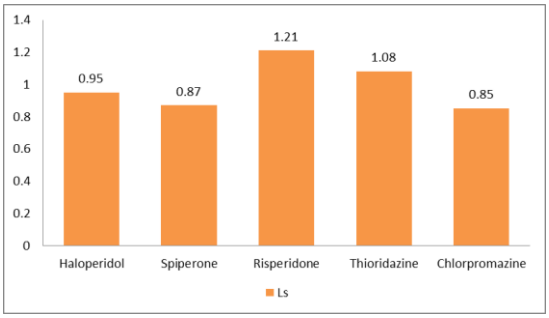

Fig. 5. Average level of dopamine in the drug

TABLE IV
L_Q, L_S, W_S AND W_Q VALUES USING STEADY STATE PROBABILITIES

DRUGS	L_Q	L_S	W_Q	W_S
HALOPERIDOL	0.334415	0.9551478	0.1393397	0.397978254
SPIPERONE	0.4201157	0.879981716	0.0503937	0.184096811
RISPERIDONE	0.396088	1.21692837	0.1650368	0.452886824
THIORIDAZINE	0.457992	1.082182086	0.0248133	0.224478163
CHLORPROMAZINE	0.2902427	0.85555266	0.08536551	0.251633136

In Fig. 6, x-axis represents the different types of drugs and y-axis represents, the waiting time for reaction of drug in patient.

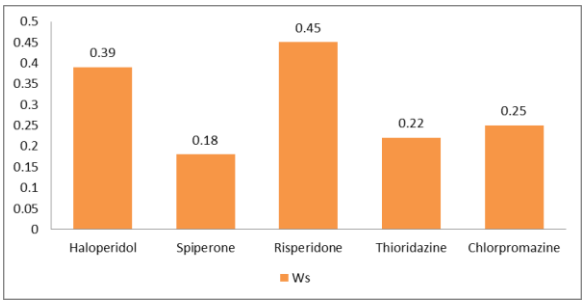

Fig. 6. Average waiting time for reaction of drug in patient

The Fig. 6, represents, the average waiting time for reaction of drug in patient. In which, level of dopamine is high in Risperidone. Haloperidol is the second highest drug. Spiperone is the drug with least level of dopamine.

Hence the two figure illustrates us that, more the level of dopamine in the drug, the more the reaction of the drug in patients. From this we conclude that, the drug Risperidone is the most safe and effective medicine to the patients. In Fig. 7, x-axis represents the different types of drugs and y-axis represents, the average level of increase of dopamine in the drug.

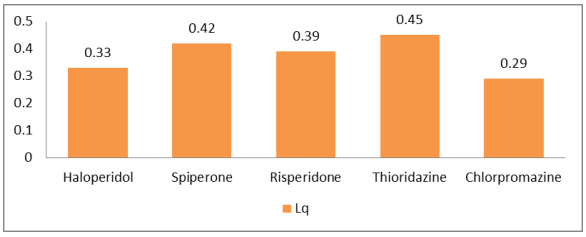

Fig. 7. Average level of increase of dopamine in the drug

The Fig. 7 displays, the increase in level of dopamine in the drug. In which, level of dopamine is high in Thioridazine. Spiperone is the second highest drug. Chlorpromazine is the drug with least level of dopamine. In Fig. 8, x-axis represents the different types of drugs and y-axis represents, the waiting time for reaction of patient while increase of dopamine in drug.

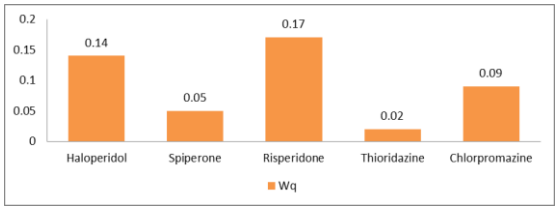

Fig. 8. Average waiting time for reaction of patient while increase of dopamine in drug

The Fig. 8 protrays, the waiting time for the reaction of patients after increasing the level of dopamine in the drug. In which, level of dopamine is high in Risperidone. Haloperidol is the second highest drug. Thioridazine is the drug with least level of dopamine.

Thus the Fig. 7 and Fig. 8 interpret us that, even if the level of dopamine is higher in Thioridazine drug, it has the least reaction of drug in patients. From this we terminate that, the drug Thioridazine is least effective and is not a safe medicine.

IV. Conclusion

We have taken a receptor from neurotransmission of nerve cells in Brain called as Dopamine receptors, which plays a vital role in reward, motivation memory, and attention and body movements. When a person is lacking in the above terms they use the drugs to increase the level of dopamine receptors in the Brain. Here we analysed five types of drugs and given the best out of five and the least which should not be prescribed. We analyzed both transient state as well as steady state to find the result. Also, it has been found that in both the state we get the result as drug called Risperidone is the best drug to use with very less side effects and the drug called Thioridazine has very high side effects and it has less reaction in increase of dopamine level in patients.

Comparing Transient state and Steady state results, we conclude that in both the states, medicine called Risperidone has the highest reaction in patients than that of other drugs even if the level is increased in small amount it gives the most high in reaction. Also, in both the cases Thioridazine is the medicine with the least reaction and has much side effects.

Thus, we recommend the patients to use the drug Risperidone, which is the most safe and effective medicine.

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