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MONOAMINE OXIDASE-A ENZYME ON KINTAMANI DOGS IN BALI, INDONESIA

Ensim Monoamin Oksidase-A Anjing Kintamani Di Bali Indonesia

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Abstract

The enzyme monoamine oxidase-A (MAO-A) is a compound that can break down serotonin. So if the level of monoamine oxidase-A in the blood is high, the level of serotonin in the blood will be low. It is known that the enzyme monoamine oxidase-A affects dog aggression. How exactly is the picture of monoamine oxidase-A in the blood of pet dogs has not been widely revealed. The purpose of this study was to determine the levels of monoamine oxidase-A in Kintamani pet dogs. Kintamani dogs are a native Indonesian dog breed found in Kintamani Village, Bali Province, Indonesia. The study used forty dogs, 15 male dogs and 15 female dogs and 10 lactating dogs. The method used in this study was the observation and cross-sectional sampling method and monoamine oxidase-A levels were determined using the elisa technique. The results showed that the average levels of monoamine oxidase-A in male Kintamani dogs (ng/ml) were 3.54 ± 1.9, females 4.85 ± 1.7 and lactating dogs 3.15 ± 2.23. The conclusion that monoamine oxidase-A level depending sex and lactating. The levels of monoamine oxidase in male dogs are lower than in female and lactating dogs. It is recommended to conduct research on the levels of monoamine oxidase A in Kintamani dogs that behave aggressively.

Keywords: enzyme; monoamine oxidase-A; blood; dog

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Abstrak

Enzim monoamine oxidase-A (MAO-A) merupakan senyawa yang dapat memecah serotonin. Jadi apabila kadar monoamine oxidase-A dalam darah tinggi maka kadar serotonin dalam darah akan rendah. Diketahui bahwa enzim monoamine oxidase-A mempengaruhi agresivitas anjing. Bagaimana sebenarnya gambaran monoamine oxidase-A dalam darah anjing peliharaan belum banyak terungkap. Tujuan dari penelitian ini adalah untuk mengetahui kadar monoamine oxidase-A pada anjing peliharaan Kintamani. Anjing Kintamani merupakan ras anjing asli Indonesia yang terdapat di Desa Kintamani, Provinsi Bali, Indonesia. Penelitian menggunakan empat puluh ekor anjing, 15 ekor anjing jantan dan 15 ekor anjing betina serta 10 ekor anjing laktasi. Metode yang digunakan dalam penelitian ini adalah metode observasi dan cross-sectional sampling dan kadar monoamine oxidase-A ditentukan dengan menggunakan teknik elisa. Hasil penelitian menunjukkan bahwa rata-rata kadar monoamine oxidase-A pada anjing Kintamani jantan (ng/ml) adalah 3,54 ± 1,9, betina 4,85 ± 1,7 dan anjing laktasi 3,15 ± 2,23. Kesimpulannya adalah kadar monoamine oxidase-A tergantung pada jenis kelamin dan masa menyusui. Kadar monoamine oxidase pada anjing jantan lebih rendah dibandingkan pada anjing betina dan masa menyusui. Disarankan untuk melakukan penelitian tentang kadar monoamine oxidase A pada anjing Kintamani yang berperilaku agresif.

Kata kunci: enzim; monoamine oxidase-A; darah; anjing.

INTRODUCTION

Monoamine oxidase-A (MAO-A) is an enzyme that breaks down serotonin and is produced by the outer membrane of mitochondria. MAO-A catalyzes the oxidation of primary, secondary, and tertiary amines, including several neurotransmitters, into their corresponding amines. It plays a key role in breaking down serotonin (5-hydroxytryptamine), epinephrine, and norepinephrine (Edmondson et al., 2004; Youdim and Riederer, 2011; Gupta et al., 2015; Prah et al., 2020). During its activity, MAO-A produces hydrogen peroxide (H_2O_2), which can damage nearby cellular molecules. Oxidative stress resulting from this H_2O_2 tends to be higher in glial cells than in neurons due to the greater diffusion of amines from the synaptic cleft (Binda et al., 2011). The physiological impact of such oxidative stress has been studied in the heart, where MAO-A activity in cardiomyocytes is considered significant (John and Jose, 2016).

Several studies have explored the association between MAO-A and aggression, with mixed results in both human and animal models (Dorfman et al., 2014; Du et al., 2004; Fergusson et al., 2012; Gallardo et al., 2013; Huang et al., 2009; Kolla et al., 2020; McDermott et al., 2009; Vishnivetskaya et al., 2007; Yu et al., 2005; Schulze et al., 2000). Cases et al. (1995) found that aggressive mice had lower levels of MAO-A than non-aggressive ones. Shih et al. (1999) suggested that MAO-A plays a role under stress conditions and that its deficiency can make organisms more vulnerable to environmental substances, drugs, or biogenic amines. Prah et al. (2020) added that high MAO-A activity, coupled with an active serotonin transporter, can lead to decreased serotonin and norepinephrine levels, often linked to depression, anxiety, and other mood disorders. Conversely, low MAO-A activity may cause increased levels of these neurotransmitters, affecting brain plasticity during prenatal neurogenesis. Meyer et al. (2006) reported that MAO-A levels were elevated by an average of 34% in the brains of patients with major depressive disorder. Gallardo-Pujol et al. (2013) found higher aggression levels in individuals with low-activity MAO-A variants. However, other studies, such as those by Huang (2009) and Tiihonen et al. (2015), failed to establish a significant link between MAO-A and either major depressive disorder or aggression.

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Regardless of the pros and cons about the relationship between MAO-A and aggressive behavior, we tried to examine the natural MAO-A levels in native Indonesian dogs, namely Kintamani dogs. This was done because studies on Kintamani dogs have not been widely conducted.

RESEARCH METHODS

Ethical Clearance

This research has received approval from the ethics commission with reference number: B/246/UN14.2.9/PT.01.04/2024.

Research Object

This study used 40 dogs including 15 males, 15 females and 10 lactating. All dogs were observed clinical symptoms and physically healthy. The dogs come from Sukawana village, Kintamani sub-district, Bangli district, Bali, Indonesia. Determination of monoamine oxidase levels using the Elisa technique.

A 3-mL blood sample was collected from the saphena vein of each dog into anticoagulant (EDTA) tubes. Samples were centrifuged at 1500 x g (or 3000 rpm) at 28 ^{0}C within 10 minutes. Plasma was frozen and stored at -20 ^{0}C until its analysis. Monoamine oxidase A ELISA kit (MyBioSource Southern California, San Diego (USA) with Cat.No: MBS9368907 was used to measure monoamine oxidase A levels in plasm.

Research Design

This study uses an observational design with cross-sectional sampling. Sampling was carried out using a purposive system.

Research Variables

Research Variables are including dogs as independent variables (with tree independent variables: male, female and lactating), monoamine oxidase A levels as dependent variables, breed, age and origin of dogs as control variables.

Data Collection Methods

The data collection method was carried out by taking blood samples from the saphenous vein using a 3 ml syringe and then collected into an EDTA anticoagulant tube. After being homogenized for 30 seconds, the tube was put into a cool box. Then the blood sample was examined using the ELISA technique.

Data analysis

Anova test and Duncon's test were used in this study to determine differences between variables (Steel and Torri, 1981). A value of $P \leq 0.05$ was considered significant for all analyses. Data were analyzed using statistical software for Windows (SPSS).

RESULTS AND DISCUSSION

Result

Full results are presented in Table 1. The table presents the concentration of monoamine oxidase A (ng/ml) across different groups of Kintamani dogs. Male subjects exhibited a mean concentration of 3.54 ng/ml with a standard deviation of 1.9, labeled with the superscript "a". Female subjects showed a higher mean concentration of 4.85 ng/ml with a standard deviation of 1.7, denoted by a different superscript "b", indicating a statistically significant difference from the male group. Lactating individuals had a mean concentration of 3.15 ng/ml with a standard deviation of 2.23, sharing the superscript "a" with males, suggesting no significant

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difference between these two groups. Levels of monoamine oxidase a in Kintamani dogs is presenting in Graph 1.

Discussion

Monoamine oxidase levels in males, females and lactating showed significant differences ($P < 0.05$). Duncan's test showed that the levels of monoamine oxidase A in males were significantly ($P < 0.05$) lower than those in females and breastfeeding, whereas in females they were not significantly different ($P > 0.05$) with breastfeeding. The results showed that monoamine oxidase A levels in male and lactating dogs were significantly lower than female dogs ($P <0.05$).

Regarding MAO-A and aggressive behavior, aggressive dogs have lower MAO-A levels. And it is known that in general nursing dogs and male dogs have more aggressive behavior than female dogs. These results are different from the findings of Meyer, et al., (2006) on mice, that there was a significant increase in MAO-A in all brain regions in the depression group compared to the healthy group. Likewise Naoi, et al., (2018) argues that in depressive disorders, there is an increase in MAO-A expression and a decrease in serotonin in the brain. However, the results of our study support research conducted by Cases, et al., (1995), that deficiency of monoamine oxidase A (MAO-A) in the brain causes increased aggressiveness. Likewise Chen and Shih, (1997) argue that rats lacking MAO-A show increased levels of serotonin and aggressive behavior. On the other hand, Bortolato and Shih, (2011) in their research on mice lacking MAO-A, showed depressive behavior.

Monoamine oxidase A (MAO-A) deficiency, associated with aggressive behavior where MAO-A regulates brain development during prenatal and postnatal maintenance. Low MAO-A will disrupt neurogenesis in the hippocampus. This will result in depression and will lead to aggression. In the stages of brain development and maturation, MAO-A modulates sensitivity to stress (Naoi et al., 2018).

Low MAO-A activity associated with higher amines has been demonstrated in studies of knockout mice and MAO-A-deficient humans. MAO-A/B knockout mice display anxiety-like symptoms of having elevated monoamines (Shih et al., 1999; Chen et al., 2004).

Despite the disagreement that the aggressive state has features of high or low monoamine oxidase A, it seems that differences in study methods influenced the results. For example, direct manipulation of monoamine oxidase A in animals or people will be different from natural monoamine oxidase A. Richardson, (1993) stated that monoamine oxidase activity helps maintain the rate of firing of neurons throughout the body within homeostatic limits. As in our study, sampling was carried out on dogs without monoamine oxidase manipulation and the animals were not in a stressful situation, but were innately (naturally) aggressive. It also seems that stressful and normal situations reflect different effects on both serotonin and monoamine oxidase.

CONCLUSION AND SUGGESTION

Conclusion

The conclusion that monoamine oxidase-A level depending sex and lactating. The levels of monoamine oxidase in male dogs are lower than in female and lactating dogs.

Suggestion

It is recommended to conduct research on the levels of monoamine oxidase A in Kintamani dogs that behave aggressively.

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REFERENCES

Binda, C., Mattevi, A., & Edmondson, D.E. (2011). Structural properties of human monoamine oxidases A and B. Monoamine Oxidase and their Inhibitors. International Review of Neurobiology. 100, 1–11. doi:10.1016/B978-0-12-386467-3.00001-7.

Bortolato, M., & Shih, J.C. (2011). Behavioral Outcomes of Monoamine Oxidase Deficiency: Preclinical and Clinical Evidence. Int Rev Neurobiol. 100, 13–42. doi: 10.1016/B978-0-12-386467-3.00002-9

Cases, O., Seif, I., Grimsby, J., Gaspar, P., Chen, K., Pournin, S., Müller, U., Aguet, M., Babinet, C., & Shih, J.C. (1995). Aggressive Behavior and Altered Amounts of Brain Serotonin and Norepinephrine in Mice Lacking MAOAA. Science, 268(5218), 1763-6. DOI: 10.1126/science.7792602.

Dorfman, H.M., Meyer-Lindenberg, A., Buckholtz, J.W. (2014). Neurobiological Mechanisms for Impulsive-Aggression: The Role Of MAO-A. Current Topics in Behavioral Neurosciences. 17, 297–313. doi:10.1007/7854_2013_272.

Du, L., Bakish, D., Ravindran, A., & Hrdina, P.D. (2004). MAO-A Gene Polymorphisms Are Associated With Major Depression and Sleep Disturbance In Males. NeuroReport. 15(13), 2097–3101. doi:10.1097/00001756-200409150-00020.

Edmondson, D.E., Mattevi, A., Binda, C., Li, M., & Hubalek, F. (2004). Structure and Mechanism of Monoamine oxidase. Journal Name: Current Medicinal Chemistry. 11(15), DOI: 10.2174/0929867043364784.

Fergusson, D.M., Boden, J.M., Horwood, L.J., Miller, A., & Kennedy, M.A. (2012). Moderating Role of The MAO-A Genotype In Antisocial Behaviour. The British Journal of Psychiatry. 200(2), 116–23. doi:10.1192/bjp.bp.111.093328.

Gallardo-Pujol, D., Andrés-Pueyo, A., & Maydeu-Olivares, A. (2013). MAO-A Genotype, Social Exclusion And Aggression: An Experimental Test Of A Gene-Environment Interaction. Genes, Brain and Behavior. 12(1), 140–5. doi:10.1111/j.1601-183X.2012.00868.x.

Gupta, V., Khan, A.A., Sasi, B.K., Mahapatra, N.R. (2015). Molecular Mechanism of Monoamine Oxidase A Gene Regulation Under Inflammation and Ischemia-Like Conditions: Key Roles of The Transcription Factors GATA2, Sp1 And TBP. Journal of Neurochemistry. 134(1), 21–38. doi:10.1111/jnc.13099.

Huang, S.Y., Lin, M.T., Lin, W.W., Huang, C.C., Shy, M.J., & Lu, R.B. (2009). Association of Monoamine Oxidase A (MAO-A) Polymorphisms And Clinical Subgroups Of Major Depressive Disorders In The Han Chinese Population. The World Journal of Biological Psychiatry. 10 (4 Pt 2), 544–51. doi:10.1080/15622970701816506.

John, P.M.F., & Jose, M.R. (2016). Inhibitors of MAO-A and MAO-B in Psychiatry and Neurology. Front Pharmacol. 7, 340. doi: 10.3389/fphar.2016.00340

Kolla NJ and Bortolato M. (2020). The Role of Monoamine Oxidase A In The Neurobiology of Aggressive, Antisocial, And Violent Behavior: A Tale Of Mice And Men. Progress in Neurobiology. 194, 101875. doi:10.1016/j.pneurobio.2020.101875.

McDermott, R., Tingley, D., Cowden, J., Frazzetto, G., & Johnson, D.D. (2009). Monoamine Oxidase A Gene (MAO-A) Predicts Behavioral Aggression Following Provocation. Proceedings of the National Academy of Sciences of the United States of America. 106(7), 2118–23. Bibcode:2009PNAS..106.2118M. doi:10.1073/pnas.0808376106.

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Meyer, J.H., Ginovart, N., Boovariwala, A., Sagrati, S., Hussey, D., & Garcia, A. (2006). Elevated Monoamine Oxidase A Levels In The Brain: An Explanation For The Monoamine Imbalance of Major Depression. Archives of General Psychiatry. 63(11), 1209–16. doi:10.1001/archpsyc.63.11.1209.

Naoi, M., Maruyama, W., & Shamoto-Nagai, M. (2018). Type a Monoamin oksidase and Serotonin are Coordinately Involved in Depressive Disorders: From Neurotransmitter Imbalance to Impaired Neurogenesis. J Neural Transm (Vienna). 125(1), 53-66. doi: 10.1007/s00702-017-1709-8.

Prah, A., Purg, M., Stare, J., Vianello, R. & Mavri, J. (2020). How Monoamine Oxidase A Decomposes Serotonin: An Empirical Valence Bond Simulation of the Reactive Step. J Phys Chem B. 124(38), 8259–8265. Doi: 10.1021/acs.jpcb.0c06502.

Schulze, T.G., Müller, D.J., Krauss, H., Scherk, H., Ohlraun, S., & Syagailo, Y.V. (2000). Association Between A Functional Polymorphism In The Monoamine Oxidase A Gene Promoter And Major Depressive Disorder. American Journal of Medical Genetics. 96(6), 801–3. doi:10.1002/1096-8628(20001204)96:6<801

Shih, J.C., Chen, K., & Ridd, M.J. (1999). Role of MAO A and B in Neurotransmitter Metabolism and Behavior. Pol J Pharmacol. 51(1), 25-29.

Steel, R.G.D., & Torrie, J.H. (1981). Principles and Procedureof Statistics. A Biometrical Approach. 2nd ed. McGraw-Hill International Book Company. N.Y.

Vishnivetskaya, G.B., Skrinskaya, J.A., Seif, I., & Popova N.K. (2007). Effect of MAO-A Deficiency on Different Kinds of Aggression And Social Investigation In Mice. Aggressive Behavior. 33 (1), 1–6. doi:10.1002/ab.20161.

Youdim MBH and Reiderer P. 2011. Monoamine oxidases and Their Inhibitors. 1st. ed. Vol. 100. Academic Press. San Diego. CA 92101-4495. USA p. 2-281.

Yu YW, Tsai SJ, Hong CJ, Chen TJ, Chen MC, Yang CW. (2005). Association Study Of A Monoamine Oxidase A Gene Promoter Polymorphism With Major Depressive Disorder And Antidepressant Response. Neuropsychopharmacology. 30(9), 1719–23. doi: 10.1038/sj.npp.1300785.

Table

Table 1. Levels of Monoamine Oxidase A in Kintamani Dogs

Variable	Monoamine oxidase A (ng/ml)
Male	3.54±1,9[a]
Female	4.85±1,7[b]
Lactating	3.15±2,23[a]

Note: superscript in the same colum shows a significant difference (P < 0,05).

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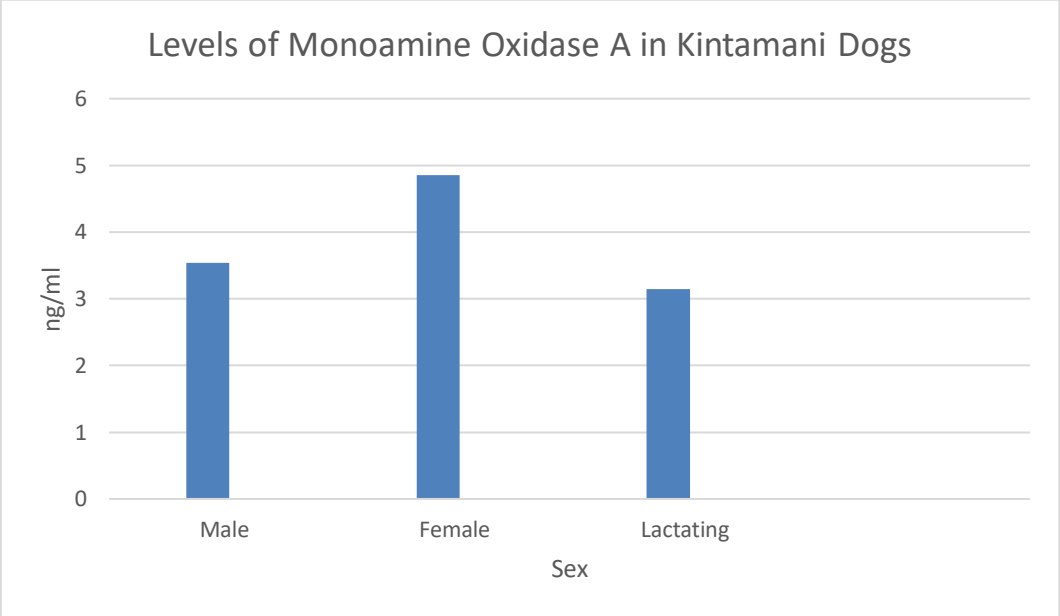
Graph



Graph 1. Levels of Monoamine Oxidase A in Kintamani Dogs

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