

Review Article

Dogs, Mental Stress and the Human Heart: Role of Cortisol and Neuropeptide Y

Devarajan Rathish^{1,2}, Rajapakse Peramune Vedikkarage Jayanthe Rajapakse¹, Kosala Gayan Abeyesundara Dissanayake Weerakoon³

Abstract

Effects of canine companionship on human cardiovascular health have been widely explored and known to be positively related. Nevertheless, the exact mechanisms related to this phenomenon are yet to be unravelled. A high level of cortisol is associated with noncommunicable diseases such as hypertension, type 2 diabetes and dyslipidaemia. Further, dog owners were found to have low cortisol levels. Interestingly neuropeptide Y (NPY), a neurotransmitter released during acute stress, increases cortisol levels. NPY has also been implicated in cardiovascular disease. We hypothesize the role of canine companionship on cardiovascular health via NPY and cortisol in a psycho-neuro-immuno-endocrine concept.

Keywords: Diabetes mellitus, dogs, dyslipidemia, hypertension, psychological stress

International Journal of Human and Health Sciences Vol. 07 No. 01 January'23 Page : 15-19
DOI: <http://dx.doi.org/10.31344/ijhhs.v7i1.491>

Introduction

"Dogs are not our whole life, but they make our lives whole," says Rodger Caras a photographer and writer. Canine companionship dates back to ancient human civilization ¹. Nowadays, companionship is a common reason for having pets, and most pet owners consider their pet a valued family member ². In addition to this psycho-social relationship, ownership is associated with some health benefits including cardiovascular health ³. Nevertheless, the exact mechanisms related to this phenomenon are yet to be unravelled. Biomarkers of stress and emotional attachment such as cortisol are investigated concerning pet ownership-related cardiovascular health ⁴⁻⁶. A systematic review revealed a significant reduction of cortisol in canine companionship and dog-assisted therapy along with a significant reduction in heart rate,

systolic blood pressure, mean arterial blood pressure, or total cholesterol level ⁷. Therefore, we hypothesize the role of canine companionship on cardiovascular health via NPY and cortisol in a psycho-neuro-immuno-endocrine concept.

The Perspective

Stress and Cardiovascular Disease

The psycho-neuro-immuno-endocrine pathway explains the role of stress in cardiovascular disease ⁸. The pathway is on the interactions between the psyche, neural and endocrine functions and immune responses. The interactions can be altered by epigenetic factors and major stressors which act via different pathways and neurotransmitters. The above alterations could lead to the emergence of disease ⁹. The risk of incident coronary heart disease increases in adults with personal or

1. Department of Veterinary Pathobiology, Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, Peradeniya, Sri Lanka.
2. Department of Family Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura, Sri Lanka.
3. Department of Parasitology, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura, Sri Lanka.

Correspondence to: Dr. D. Rathish, Department of Family Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura, Sri Lanka. E-mail: drathish@med.rjt.ac.lk. ORCID ID: 0000-0003-3346-4410.

occupational stress¹⁰. The above association is independent of familial background, history of somatic/psychiatric diseases, and psychiatric comorbidity¹¹. Further, work stress due to job strain, effort-reward imbalance, and organizational injustice is shown to contribute to coronary heart disease¹². Moreover, an individual's response to a stressor, the degree and duration of stress are influential in the independent association between stress and cardiovascular disease¹³. Therefore, a multidimensional approach is proposed in the management of multidimensional cardiovascular disease by considering stress along with the other risk factors¹⁴.

Cortisol, Neuropeptide Y and Cardiovascular Disease

A positive association between incident cardiovascular disease and morning plasma cortisol is evident through a three-method approach using a prospective nested case-control study, a meta-analysis of prospective studies and two-sample Mendelian randomization¹⁵. A high level of cortisol in a human is associated with hypertension (due to sodium retention and nitric oxide suppression)¹⁶, glucose intolerance, insulin resistance, type 2 diabetes¹⁷, endothelial damage, visceral fat accumulation, impaired lipid metabolism¹⁸, and immune modulation¹⁹. Patients with Cushing's syndrome experience high blood pressure due to an adrenocorticotrophic hormone-stimulated increase in cortisol secretion²⁰. Also, healthy men show elevated blood pressure when administered with cortisol²¹. And, 09.00 am cortisol levels were strongly associated with systolic and diastolic blood pressure values, fasting blood glucose, insulin resistance and fasting triglyceride in a South Asian cohort²². The cortisol excretion rate correlated positively with body mass index, and waist and hip measurements¹². Further, cortisol regulation has an important role in therapeutics for cardiovascular disease¹⁹. Moreover, Neuropeptide Y (NPY) stimulates cortisol secretion thereby potentiating the effects of cortisol on cardiovascular disease²³.

NPY is a 36 amino-acid peptide that is expressed widely in the central nervous system, with a wide variety of functions at different neuroanatomic locations²⁴. The current discussion focuses mostly on its expression in the limbic system, brainstem, and hypothalamus, as those areas are thought to be important for NPY's role in regulating emotional-affective behaviour, stress coping and feeding²⁵.

It is released during acute stress, serving roles in anxiolysis and neuroprotection. NPY increases appetite, vasoconstriction, blood pressure, atherosclerotic plaque formation, arrhythmia²⁶, and total and low-density lipoprotein cholesterol²⁷. Also, it is involved in immune modulation²⁶. Therefore, NPY is associated with feeding disorders, hypertension and cardiovascular disease²⁶. Further, NPY regulation has an important role in therapeutics for cardiovascular disease similar to cortisol²⁸. Moreover, NPY and its receptors are prospects for the clinical intervention of metabolic syndrome²⁹.

Canine Companionship and Cardiovascular Disease

Protection against coronary artery disease is an epiphenomenal benefit of canine companionship. Dog ownership could buffer the autonomic responses³⁰ and achieve higher heart rate variability³¹ in patients with diabetes mellitus, hypertension and hyperlipidemia. Improved survival in myocardial infarction is seen among elderly pet owners³². Also, it has been shown that dog owners who regularly walked their dogs had a lower chance of self-reported hypertension, diabetes and hypercholesterolemia compared to non-dog owners³³. The above could be due to the secondary effect of improved physical activity associated with canine companionship. Further, dog owners exhibit higher high-density lipoprotein which might be due to increased physical activity among them³⁴. Moreover, pet ownership is associated with lower levels of serum triglycerides³⁵ and low-density lipoprotein³⁶.

Low cortisol levels are found in dog-assisted therapy and dog ownership which provides evidence for the acute and long-term influence of canine companionship on human cortisol levels. A high level of cortisol leads to an increase in the risk factors for cardiovascular disease. Also, NPY increases cortisol levels. Both cortisol and NPY are released during acute stress and have been implicated in cardiovascular disease. If canine companionship reduces mental stress, it would potentially reduce the expression of NPY and decrease the cortisol level. Therefore, following the psycho-neuro-immuno-endocrine concept, we hypothesize (Figure 1) that canine companionship reduces stress and could decrease: (A) NPY level, (B) cortisol level, and (C) NPY-induced potentiation of cortisol levels. The net effect would be a reduction in the end processes that contribute to cardiovascular disease.

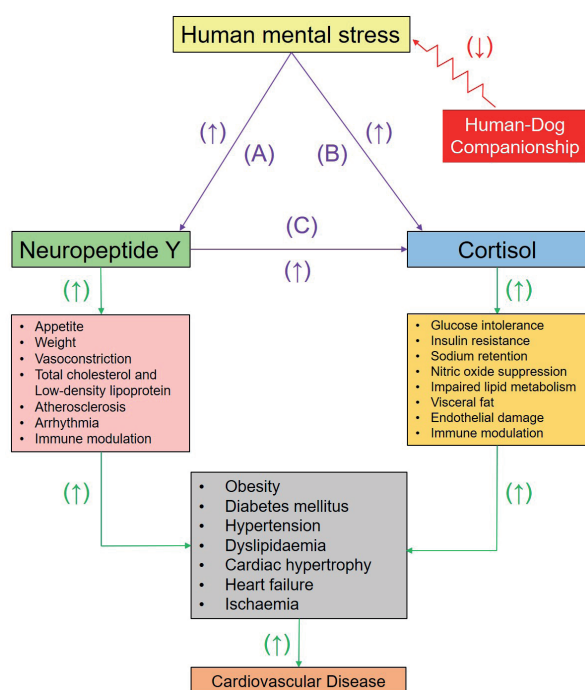


Figure 1. The hypothetical role of canine companionship on cardiovascular health via human neuropeptide Y (NPY) and cortisol: a psycho-neuro-immuno-endocrine effect.

Canine companionship reduces stress and could decrease: (A) NPY level, (B) cortisol level, and (C) NPY-induced potentiation of cortisol level. The net effect would be a reduction in the end processes that contribute to cardiovascular disease

Highlights

Effects of canine companionship on human cardiovascular health have been widely explored and known to be positively related. Nevertheless, the exact mechanisms related to this phenomenon are yet to be unravelled. A high level of cortisol is associated with noncommunicable diseases such as hypertension, type 2 diabetes and dyslipidaemia. Interestingly neuropeptide Y (NPY), a neurotransmitter released during acute stress, increases cortisol levels. NPY has also been implicated with cardiovascular disease.

We hypothesize the role of NPY along with cortisol towards the association between canine companionship and cardiovascular health in a psycho-neuro-immuno-endocrine concept.

Outlook for future research

A community-based, comparative cross-sectional study or higher-level studies with laboratory analysis could be conducted among pet dog owners and, age, and matched individuals who do not own a pet. The effect of canine companionship can be evaluated by comparing mental stress, anthropometric measurements, human NPY, cortisol and cardiovascular health indices in the above two groups. Also, a pre-post study with dog-assisted therapy could be conducted among healthy volunteers or patients with cardiovascular diseases to compare their serum NPY, cortisol and cardiovascular health indices before and after the intervention. However, canine companionship or dog-assisted therapy is proposed only as a complement to well-established cardiovascular treatment and preventive measures. Also, dog ownership is not proposed for the primary purpose of reducing cardiovascular disease risk.

Abbreviations

NPY - Neuropeptide Y

LDL - Low-density lipoprotein

Conflict of interest: The authors declare no conflict of interest concerning the financial interests, personal relationships, authorship and/or publication of this article.

Funding statement: No funding.

Ethical clearance: Not applicable.

Authors' contribution: DR conceived the idea and conducted the literature survey. DR drafted the manuscript while JR and KW critically revised it. DR prepared figure 1. All authors read and approved the final manuscript.

References

1. Case L. ASAS Centennial paper: Perspectives on domestication: The history of our relationship with man's best friend. *J Anim Sci*. 2008;86(11):3245–51.
2. Walsh F. Human-Animal Bonds II: The Role of Pets in Family Systems and Family Therapy. *Fam Process*. 2009;48(4):481–99.
3. Xie Z-Y, Zhao D, Chen B-R, Wang Y-N, Ma Y, Shi H-J, et al. Association between pet ownership and coronary artery disease in a Chinese population. *Medicine (Baltimore)*. 2017;96(13):e6466.
4. Delgado C, Toukonen M, Wheeler C. Effect of Canine Play Interventions as a Stress Reduction Strategy in College Students. *Nurse Educ*. 2018;43(3):149–53.
5. Krause-Parello CA, Levy C, Holman E, Kolassa JE. Effects of VA Facility Dog on Hospitalized Veterans Seen by a Palliative Care Psychologist: An Innovative Approach to Impacting Stress Indicators. *Am J Hosp Palliat Med [Internet]*. 2018;35(1):5–14.
6. Morales-Jinez A, López-Rincón FJ, Ugarte-Esquivel A, Andrade-Valles I, Rodríguez-Mejía LE, Hernández-Torres JL. Allostatic load and canine companionship: a comparative study using biomarkers in older adults. *Rev Lat Am Enfermagem*. 2018;26.
7. Rathish D, Rajapakse RPVJ, Weerakoon KGAD. The role of cortisol in the association of canine-companionship with blood pressure, glucose, and lipids: a systematic review. *High Blood Press Cardiovasc Prev*. 2021;28(5):447–55.
8. Fioranelli M, Bottaccioli AG, Bottaccioli F, Bianchi M, Rovesti M, Rocchia MG. Stress and Inflammation in Coronary Artery Disease: A Review Psychoneuroendocrineimmunology-Based. *Front Immunol*. 2018;9.
9. González-Díaz SN, Arias-Cruz A, Elizondo-Villarreal B, Monge-Ortega OP. Psychoneuroimmunoendocrinology: clinical implications. *World Allergy Organ J*. 2017;10(1):19.
10. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. *Nat Rev Cardiol*. 2018;15(4):215–29.
11. Song H, Fang F, Arnberg FK, Mataix-Cols D, Fernández de la Cruz L, Almqvist C, et al. Stress related disorders and risk of cardiovascular disease: population based, sibling controlled cohort study. *BMJ*. 2019;11255.
12. Fraser R, Ingram MC, Anderson NH, Morrison C, Davies E, Connell JM. Cortisol effects on body mass, blood pressure, and cholesterol in the general population. *Hypertens (Dallas, Tex 1979)*. 1999;33(6):1364–8.
13. Dar T, Radfar A, Abohashem S, Pitman RK, Tawakol A, Osborne MT. Psychosocial Stress and Cardiovascular Disease. *Curr Treat Options Cardiovasc Med*. 2019;21(5):23.
14. Morera LP, Marchiori GN, Medrano LA, Defagó MD. Stress, Dietary Patterns and Cardiovascular Disease: A Mini-Review. *Front Neurosci*. 2019;13.
15. Crawford AA, Soderberg S, Kirschbaum C, Murphy L, Eliasson M, Ebrahim S, et al. Morning plasma cortisol as a cardiovascular risk factor: findings from prospective cohort and Mendelian randomization studies. *Eur J Endocrinol*. 2019;181(4):429–38.
16. Kelly JJ, Mangos G, Williamson PM, Whitworth JA. Cortisol and hypertension. *Clin Exp Pharmacol Physiol Suppl*. 1998;25:S51–6.
17. Siddiqui A, Madhu S V, Sharma SB, Desai NG. Endocrine stress responses and risk of type 2 diabetes mellitus. *Stress*. 2015;1–9.
18. Di Dalmazi G, Pasquali R, Beuschlein F, Reincke M. Subclinical hypercortisolism: a state, a syndrome, or a disease? *Eur J Endocrinol*. 2015;173(4):M61–71.
19. van der Sluis RJ, Hoekstra M. Glucocorticoids are active players and therapeutic targets in atherosclerotic cardiovascular disease. *Mol Cell Endocrinol*. 2020;504:110728.
20. Whitworth JA, Williamson PM, Mangos G, Kelly JJ. Cardiovascular consequences of cortisol excess. *Vasc Health Risk Manag*. 2005;1(4):291–9.
21. Connell JM, Whitworth JA, Davies DL, Lever AF, Richards AM, Fraser R. Effects of ACTH and cortisol administration on blood pressure, electrolyte metabolism, atrial natriuretic peptide and renal function in normal man. *J Hypertens*. 1987;5(4):425–33.
22. Ward AM V, Fall CHD, Stein CE, Kumaran K, Veena SR, Wood PJ, et al. Cortisol and the metabolic syndrome in South Asians. *Clin Endocrinol (Oxf)*. 2003;58(4):500–5.
23. Antonijevic IA, Murck H, Bohlhalter S, Frieboes RM, Holsboer F, Steiger A. Neuropeptide Y promotes sleep and inhibits ACTH and cortisol release in young men. *Neuropharmacology*. 2000;39(8):1474–81.
24. Wahlestedt C, Ekman R, Widerlöv E. Neuropeptide Y (NPY) and the central nervous system: distribution effects and possible relationship to neurological and psychiatric disorders. *Prog Neuropsychopharmacol Biol Psychiatry*. 1989;13(1–2):31–54.
25. Reichmann F, Holzer P. Neuropeptide Y: A stressful review. *Neuropeptides*. 2016;55:99–109.
26. Tan CMJ, Green P, Tapoulal N, Lewandowski AJ, Leeson P, Herring N. The Role of Neuropeptide Y in Cardiovascular Health and Disease. *Front Physiol*. 2018;9.
27. Uusitupa MI, Karvonen MK, Pesonen U, Koulu M. Neuropeptide Y: A novel link between the neuroendocrine system and cholesterol metabolism. *Ann Med*. 1998;30(6):508–10.
28. Brothers SP, Wahlestedt C. Therapeutic potential of

- neuropeptide Y (NPY) receptor ligands. *EMBO Mol Med.* 2010;2(11):429–39.
29. Huang Y, Lin X, Lin S. Neuropeptide Y and Metabolism Syndrome: An Update on Perspectives of Clinical Therapeutic Intervention Strategies. *Front Cell Dev Biol.* 2021;9.
 30. Aiba N, Hotta K, Yokoyama M, Wang G, Tabata M, Kamiya K, et al. Usefulness of Pet Ownership as a Modulator of Cardiac Autonomic Imbalance in Patients With Diabetes Mellitus, Hypertension, and/or Hyperlipidemia. *Am J Cardiol.* 2012;109(8):1164–70.
 31. Friedmann E, Thomas SA, Stein PK, Kleiger RE. Relation between pet ownership and heart rate variability in patients with healed myocardial infarcts. *Am J Cardiol.* 2003;91(6):718–21.
 32. Friedmann E, Thomas SA. Pet ownership, social support, and one-year survival after acute myocardial infarction in the Cardiac Arrhythmia Suppression Trial (CAST). *Am J Cardiol.* 1995;76(17):1213–7.
 33. Lentino C, Visek AJ, McDonnell K, DiPietro L. Dog walking is associated with a favorable risk profile independent of moderate to high volume of physical activity. *J Phys Act Health.* 2012;9(3):414–20.
 34. Maugeri A, Medina-Inojosa JR, Kunzova S, Barchitta M, Agodi A, Vinciguerra M, et al. Dog Ownership and Cardiovascular Health: Results From the Kardiovize 2030 Project. *Mayo Clin Proc Innov Qual Outcomes.* 2019;3(3):268–75.
 35. Dembicki D, Anderson J. Pet Ownership May Be a Factor in Improved Health of the Elderly. *J Nutr Elder.* 1996;15(3):15–31.
 36. Krittawong C, Kumar A, Wang Z, Jneid H, Virani SS, Levine GN. Pet Ownership and Cardiovascular Health in the US General Population. *Am J Cardiol.* 2020;125(8):1158–61.
-