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Norepinephrine Content in Brainstem and Hypothalamic Nuclei of Borderline and Wistar-Kyoto Rats Consuming High Salt for Varying Durations

J.E. Lawler

Norepinephrine Content in Brainstem and Hypothalamic Nuclei of Borderline and Wistar-Kyoto Rats Consuming High Salt for Varying Durations.

R. Finkel, I.P. Edgemon, G.-P. Zheng,
N.E. Dobson, and J.E. Lawler*.

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Introduction:

Both electrolytic lesions and electrical stimulation of the brain are classic methods for examining the role of the central nervous system (CNS) in control of cardiovascular function. For example, Doba and Reis (13) showed that bilateral electrolytic lesions of the nuclei tracti solitarii (NTS) in the rat at the level of the obex result in an immediate and marked elevation in arterial blood pressure. Death typically results in a matter of days. Ernsberger, Azar and Azar (14) revealed that radiofrequency lesions of the paraventricular and suprachiasmatic nuclei prevented a rise in blood pressure (BP) in salt-sensitive rats fed a high salt (8%) diet for 15 weeks. Electrical stimulation of the C1 region of the rostral ventrolateral medulla (RVLM) elicits a pressor response (46). More recently, newer techniques in the brain sciences, originally developed in the study of other neural systems, have been applied to central control of cardiovascular function. For example, microinjection of the excitatory amino acid glutamate into catecholamine-containing neurons of the RVLM produces an increase in blood pressure (36). A couple of points worth developing further are, first, that norepinephrine (NE) appears to be an important neurotransmitter in control of cardiovascular function and, second, that many of the structures studied receive direct or indirect projections from limbic system structures. Thus, there is the possibility that stressors might alter cardiovascular function sufficiently to lead to a disease state such as hypertension. However, as we shall see, this is a fairly new area of research, and results are far from conclusive.

Many years ago, Hilton (20) revealed the importance of the hypothalamus in the cardiovascular component of the fight-or-flight response. It is noteworthy that many hypothalamic nuclei contain NE and interact extensively with brainstem structures that eventually form the final common pathway to the intermediolateral cell column of the spinal cord, the point of origin of preganglionic sympathetic nervous system neurons. For example, Bennaroch et al (4) showed that reduction of NE in the anterior hypothalamus induced an increase in arterial BP and heart rate, while clonidine, an NE agonist, administered after NE depletion caused hypotension in Wistar-Kyoto (WKY) rats. This suggests that NE has a tonic

depressor effect in the anterior hypothalamus. However, NE does not always have an inhibitory effect as was shown in the study of Bachelard et al (3), where microinjection of NE into the paraventricular nuclei of Long-Evans rats produced dose-dependent increases in BP, suggesting that NE in this nucleus may contribute to elevated BP. Because of those opposing effects in different hypothalamic nuclei, assays of whole brain regions for NE (such as the Glowinski technique) may not be appropriate. This suggests a need to focus on specific brain regions.

Although the above studies utilizing microinjection techniques suggest that NE has a role in BP regulation, they do not show how a stressor might affect the CNS-BP relationship. Wintemitz and Oparil (56) showed that a high salt diet caused an increase in BP in spontaneously hypertensive rats (SHR) and also suggested that the change in sodium balance might influence central noradrengeric activity. Wintemitz et al (57) also found that by feeding young SHRs a high sodium diet, they incurred worsening hypertension and increased NE content in the anterior and dorsomedial hypothalamic nuclei which suggested that sodium and the CNS, mainly the areas controlling the sympathetic nervous system, work together to have an effect on the long-term control of blood pressure in the SHR. Pawloski-Dahm and Gordon (43) also found that increased dietary NaCl augments the pressor response of the RVLM that may have led to the increases in arterial pressure that were seen. Other stressors, including drugs such as phenylephrine (5), also showed effects on both BP and CNS neurotransmitter levels. As acute hypertension was induced by phenylephrine, WKY and SHR reacted differently with SHRs showing increased extracellular 5-hydroxyindoleacetic acid (5-HIAA) while WKY showed increased NE and 5-HIAA levels in the NTS. Nakata et al (39) also showed a correlation between a behavioral stressor and NE in their study utilizing shaker stress. This stress elicited pressor responses that were coupled with increases in dialysate NE from both the paraventricular nuclei of the hypothalamus (PVH) and the posterior hypothalamus (PH) in a frequency-dependent manner. These and other experiments suggest a role for central NE levels in BP control.

To study environmental stressors, such as those mentioned above, which have impacts on stress-induced BP responses and in causing hypertension, the borderline hypertensive rat (BHR) has become an invaluable investigative tool. The BHR is the F1 cross between the SHR and WKY, which gives it a genetic predisposition to the development of hypertension, long held to be an important factor in causing hypertension in both rats and humans. This model normally has a resting BP around 140-160 mmHg at 4 months of age that shows no further age-related increases in BP (28). Yet, when faced with shock-shock conflict stress (29) or a high salt diet (30), BHRs become hypertensive, making them a good model for environmental stress effects and genetics (reviewed in 49).

The studies mentioned above, along with others, show that stress has an effect on BP; yet, they do not show how environmental stressors affect NE levels. One such study was done by Tanaka et al (51), who used immobilization, electric foot-shock, psychological stress, and a conditioned fear paradigm as stressors, and found reductions in NE levels in most regions of the brain along with increased NE release in extended brain regions (exact regions were not mentioned). In a separate experiment, they also found increases in 3-methoxy-4-hydroxyphenylethyleneglycol sulfate, the major metabolite of NE, in the hypothalamus, pons and medulla oblongata, basal ganglia, and other regions as induced by immobilization stress (52), while immobilization produced duration-dependent effects in specific hypothalamic nuclei with decreases in NE in some nuclei after 20 minutes of stress and increases in NE levels after 40 minutes.

Since the BHR is a good model for hypertension, it also becomes a good model for studying the effects of stressors on NE content in the brain regions concerned with BP regulation. An early examination of NE content in discrete brain nuclei, especially those of the brainstem and hypothalamus, was done by Mitchell and Lawler (37), in which brain NE levels of acutely and chronically stressed BHRs and their age-matched, unstressed controls were compared. The varying durations of stress were shown to affect NE levels differently in the

brainstem and hypothalamus. This result was also obtained in a later study (31) in which compound stressors (e.g., salt and stress) were used.

The above studies, which are the basis for the present study, showed the changing effects of acute, chronic, or compound stress on NE levels in the BHR. Lawler et al (26) showed the effects of conflict stress on BP and another study (27) showed the effects of a high salt diet on BP; however, none has examined the effects of a high salt diet alone on NE levels in discrete brain nuclei. These experiments suggest that there may be a role for NE in hypertension, and the experiment of Lawler et al (28) especially implies again that salt has a role in causing hypertension and altering NE levels in discrete nuclei of the hypothalamus and brainstem. However, the duration of this experiment (two months and six months) was too long to see the effects of the stress as hypertension developed; rather, at the point where punches were taken, hypertension had already developed fully. For this reason, the schedule of diet that was used in our laboratory previously (27) which showed the increases in BP as hypertension developed as well as when it had become asymptotic (by the fourth week of the diet) was utilized in this experiment. Of particular interest in the present study, however, was to determine whether alterations in CNS levels of NE occur before hypertension develops, and whether these alterations are different in strains that have previously been shown by us and others to remain normotensive (WKY) or become hypertensive (BHR) when fed a high salt diet. Since previous studies have shown that this hypertension reaches asymptote after 4 weeks of high salt in the BHR, and since we were interested in the CNS changes occurring before hypertension onset, the current study examined NE levels in discrete brainstem and hypothalamic nuclei after 0, .5, 1, 2, 4, or 8 weeks of high salt diets in WKY and BHR. The long-range hypothesis guiding this research is that there are neural-renal interactions in the development of hypertension in the BHR. The neural component was expected, and has been confirmed by us and others, for stress, but was not anticipated for a high salt diet. However, several studies have suggested a role for the CNS in the case of high salt intake, leading us to investigate CNS changes as salt-induced hypertension develops. The nuclei chosen for investigation are those previously

studied. All have a direct (via sympathetic nervous system activation) or indirect (via hormonal influences on the blood vessels and/or alterations in renal function) role in altering blood pressure. The current presentation deals with the CNS aspects of this study. This is the part for which I had direct responsibility.

Methods and Materials

Wistar-Kyoto (WKY) rats (n=40) and borderline hypertensive rats (BHR) (n=28) were obtained from Taconic Farms, Germantown, NY. They were housed two to three per cage in a twelve hour light-dark cycle. Rats of both strains were separated into one of six categories based on duration and type of diet. Control animals were maintained on normal (1%) salt diets throughout the experiment. The experimental animals were placed on a high salt diet (8%) for either .5, 1, 2, 4, or 8 weeks. These diets were started such that all the durations ended when the animals were twelve to thirteen weeks of age. Water and rat chow were provided ad libitum.

After the cessation of the diet, all animals underwent the same surgical protocols for monitoring of blood pressure and renal function (data presented elsewhere). Once these data were obtained, approximately one week after the completion of the experimental diets, the animals were killed by decapitation, and their brains were removed and quickly frozen on dry ice. They were then stored at -80C until later tissue samples were obtained.

Eight hours before slicing, the brains were removed from the freezer and placed in a -10C cryostat to allow for some thawing. Then the brains were mounted and sliced. Utilizing the stereotaxic atlas of Paxinos and Watson (42) and a dissecting microscope, selected 300 um sections were placed on cold glass slides.

After all the slices had been obtained, brain punches of the relevant nuclei were taken using a .5 mm diameter, blunt dissecting needle according to the technique of Palkovits (36). The punches, A2, A1, C1, LC, Post, Arc, DMH, LH, VMH, PVH, Ant, SO, all bilateral except for the medial A2 punch, were then placed in microvials containing 100 ul of 3,4-

dihydroxybenzylamine hydrobromide (DHBA) and 1.0 N perchloric acid (PCA) and stored at -80C until sonication.

Samples were sonicated in a cold water bath for 3 minutes at a setting of 5 (Branson Instruments). Vials were then centrifuged at 8000 rpm for 10-15 minutes to pack the protein. The supernatant was then removed with a sterile micropipette, transferred to autoinjector vials, loaded into a Waters WISP 710B autoinjector, and injected into a high performance liquid chromatograph with an electrochemical detector to obtain the amount of NE present in the sample. Supernatant was autoinjected into the HPLC at a volume of 75 ul. A propanol-based mobile phase was carried through the system at 1 ml/min by a Waters 510 pump. Catecholamine separations were made using a reverse-phase column by Phenomenex. NE was detected by a dual series cell and BAS LC-4B amperometric detector. Data were integrated by a Hewlett-Packard 3390A Integrator. The pellets were allowed to open-air dry for approximately 24 hours and then underwent protein assay using the Bio-Rad technique.

Using the CRUNCH statistical software, data were analyzed by two-way analysis of variance (ANOVA) and independent t-tests. All values are given as mean +/- SEM. A $p<.05$ was considered statistically significant. An effect was considered statistically marginal if $.05<p<.10$. Graphs were made using SigmaPlot.

Results

The analysis of variance revealed a main effect of strain for seven nuclei (Fig. 1), a main effect of duration for eleven nuclei (Figs 2-13) and an interaction of strain and duration in four nuclei (A2, A1, PH, SO; see Figs. 14-25). Figure 1 depicts the strain effect on NE content in the twelve nuclei selected. Significant strain differences were seen in the A2 (19 +/- 2 in the WKY, 26 +/- 4 in BHR), Arc (38 +/- 4 (WKY), 26 +/- 4 (BHR)), DMH (68 +/- 5 (WKY), 54 +/- 4 (BHR)), LH (32 +/- 2 (WKY), 26 +/- 2 (BHR)), the VMH (65 +/- 5 (WKY), 44 +/- 4 (BHR)), and PVH nuclei (70 +/- 5 (WKY), 58 +/- 5 (BHR)); marginal differences were seen in the C1 nucleus

(12 +/- 6 (WKY), 10 +/- .6 (BHR)). Seven of these eight nuclei showed higher NE content in WKY than BHR.

Strain-diet interactions were found using ANOVA and are shown in Figures 14 through 25. The remainder of this discussion will focus on these figures.

Using independent t-tests (see Figures 14-25), comparisons were made between WKY and BHR means in any given salt diet duration for each of the nuclei. For the A2 nucleus (Fig. 14), BHR had significantly lower NE content after 1 week of high salt, marginally higher content after 2 weeks, and significantly higher NE after 4 weeks compared with WKY. In the A1 nucleus (Fig. 15), BHR had significantly lower NE content at .5 and 8 weeks while showing marginally more NE at 2 and 4 weeks. There was no NE content variation between the strains in the C1 nucleus, and BHRs had only marginally higher NE content over WKY at 1 week in the LC nucleus (Fig. 16). In the PH nucleus (Fig. 17), WKY had significantly higher NE content than BHR in both the control and 8 week high salt diet and significantly lower content after 2 weeks. In the Arc and PVH nuclei (Figs.19 and 23), BHR had significantly lower NE content after 8 weeks. DMH and LH nuclei (Figs. 20 and 21) had marginally more NE in WKY than BHR after .5 weeks, and the VMH nucleus (Fig. 22) contained slightly more NE in WKY than BHR at 4 and 8 weeks. In the Ant nucleus (Fig. 24), BHR had marginally less NE content after .5 weeks and significantly more NE content after 4 weeks than WKY. In the SO nucleus (Fig. 25), BHR had significantly higher NE content after 2 weeks of high salt and significantly lower NE after 8 weeks than in WKY.

Independent t-tests were also done comparing diet durations within strain. These data are shown in the appendix as means +/- SEM.

Discussion

The main purpose of this study was to investigate the effects of high salt diets of varying duration on NE levels in discrete brain nuclei which have been shown to play a role in the regulation of blood pressure. In this respect, as the diet duration increased from .5 weeks to 8

weeks, BHR generally showed increased brainstem and hypothalamic NE levels. Though the increased brainstem NE levels were consistent with results obtained in stressor studies studying the same nuclei (37), the hypothalamic results contradicted the results previously obtained. This may suggest that salt affects the brain blood pressure centers differently than other stressors when inducing hypertension. After 1 week of high salt, NE in all brain nuclei generally decreased over the values seen at .5 weeks which may suggest that these nuclei may be secreting more NE than they are storing. This trend seemed to be attenuated at 2 weeks when NE levels increased over previous study groups. In an experiment by Winternitz et al (57), after two weeks of high sodium diet, SHRs had higher NE content in the Ant and DMH that SHRs on a normal sodium diet. This result was also true for BHRs in the control and two week experimental groups. The increase in NE levels in hypothalamic nuclei persisted into the 4 week group; however, as compared to the 2 week NE levels, the brainstem nuclei showed a decrease in NE content. After 8 weeks on the high salt diet, all nuclei in the brainstem and hypothalamus had decreased NE levels as compared with 4 week values.

In comparison to control animals, BHR on 8 week high salt diets did not have higher hypothalamic NE content. This, too, is different from the results found with compound stressors (31) where after 2 months on salt and stress, the VMH nuclei had a significantly decreased NE content, while in the present study, the VMH had a marginally higher level of NE. All high salt diet durations showed higher NE content than controls in most of the hypothalamic as well as most of the brainstem nuclei with the exception of the LC nuclei.

In the normotensive WKY, most hypothalamic nuclei in the varying diet durations showed significant increases over the controls. Interestingly, during the period (weeks 2-4) during which hypertension was developing (30), an area of the brain associated with vasodepression (as reviewed by 1), the A2 region of the NTS, had higher NE content as compared to control animals for WKYs. In the BHR, however, during the same time periods (.5,1, and 2 weeks), the A2 did not have more NE than controls; instead, the C1 nucleus, a vasoconstrictor area, showed higher NE content than control BHRs. These differences in NE

content in brainstem nuclei may suggest one way in which genetically normotensive WKY and genetically hypertensive BHR vary when trying to deal with a stressor that can induce hypertension. That may suggest that the mechanism of BP control may not be functioning properly in the BHR. The lower NE levels in the A2 suggest that this nucleus may be firing more to try to alleviate the increase in blood pressure; however, this response may not be sufficient, since BP still rises, and hypertension is maintained by 4 weeks on a high salt diet (30). This may also suggest that in an animal that is predisposed to hypertension, such as the BHR, there is a deficit or error in the way that messages from the brain are processed throughout the body which leads to hypertension when induced by an environmental stress.

Overall, in the brainstem, BHRs showed lower NE levels than WKY at .5 weeks, 1 week, and 8 weeks while it was higher at 2 and 4 weeks. The 2 week data in this experiment is similar to that found by Iwai et al (22) with Dahl salt sensitive (Dahl-S) and salt-resistant (Dahl-R). In that experiment, Dahl-S were shown to have higher NE than Dahl-R on the same diet. The 2 week results for hypothalamic nuclei in BHR versus WKY showed generally the same thing as those seen in the hypothalamus of Dahl rats in (22). In both cases, sensitive rats, BHR or Dahl-S, showed increased NE over their resistant counterparts, WKY and Dahl-R, respectively, when induced by high salt diets. However, since the Iwai et al experiment tested the whole hypothalamus and brainstem rather than specific nuclei as in the present experiment, differences in experimental method must be taken into account when comparing the results.

This experiment showed that NE levels in discrete brain nuclei change as hypertension progresses when induced by high salt, and that there are differences between strains sensitive and insensitive to salt. The increase in NE content in the vasopressive C1 area, which is the final common pathway to the intermediolateral cell column, during the onset of hypertension may mean that NE levels are critically important in the brainstem during this time; however, after hypertension has been established at 4 weeks, NE content in the hypothalamus increases over the controls, suggesting a shift in function from the brainstem to the hypothalamus.

The alterations of NE levels by high salt diets could be attributed to several mechanisms. A decrease in NE levels may be due to increased secretion of NE from stores, leading to its depletion in brain nuclei which could be tested by in vivo microdialysis (48). NE reduction may also be produced by decreased synthesis, which could be estimated by measuring the enzyme phenylethanolamine N-methyltransferase (48). Because the current study yields a quantitative value about neurotransmitter content in nuclei associated with BP control without giving any results about mechanism, the probable cause for the differences in NE content observed can not be determined.

The nuclei examined in this study (A2, A1, C1, LC, PH, Arc, DMH, LH, VMH, Ant, and SO) were shown to be sensitive to high salt. However, the design of this experiment gives little information about the functional activity and changes of the central NE system that may also be occurring. The changes seen in brain nuclei may, in fact, be indicative of other related changes which cause the animals to respond, in some way, to the stressor. For example, the observed NE level alterations may be associated with changes in the sensitivity of noradrenergic receptors, as seen in Chen et al (8), which could mean that increases or decreases in NE content do not reflect the excitation or inhibition of noradrenenrgic function. This is an important aspect to gleening the role of central NE in hypertension. Accordingly, Klangkalya et al (24) and DiBona and Jones (12) have reported that reduction in NE release induces an increase in alpha-2-adrenoreceptor number in the Ant of SHRs and that a high salt diet of 6 weeks duration increases the responsiveness of the brain alpha-receptors of the BHR. Kraft et al (25) have also reported that opioid delta receptors are also important in BP regulation and that their antagonism causes decreased systemic blood pressure in experimental SHRs. They also reported that chronic antagonism of these delta receptors caused NE levels in the hypothalamus and midbrain of animals in the experimental group to be lower than that found in the controls. Studies on the connection between NE content and the responsiveness of noradrenergic receptors and opioid receptors, if there is one, would give more detailed information, as would studies concerning NE content and secretion. To this end, studying the NE levels during the

onset of hypertension between 2 and 4 weeks may be of particular interest in discerning NE action on BP. In vivo microdialysis studies in selective nuclei could be useful in providing more definitive results about the secretion and action of NE as BP is increasing.

The present results showed changes in NE levels throughout the brainstem and hypothalamus as hypertension developed. These data represent a first step toward understanding the central link between high salt diet and hypertension in the BHR. Further studies, focussing on NE release in selected areas, are necessary to establish a cause and effect relationship.

References

1. Abboud, F. M. The sympathetic system in hypertension: State-of-the-art review. Hypertension 4(Suppl II):II-208-II-225; 1982.

2. Adell, A.; Garcia-Marquez, c.: Armario, A.; Gelpi, E. Effects of chronic stress on serotonin and noradrenaline in the rat brain. Biogen. Amines 7:19-26; 1990.

3. Bachelard, H.; Harland, D.; Gardiner, S.M.; Kemp, P.A.; Bennet, T. Regional haemodynamic effects of noradrenaline injected into the hypothalamic paraventricular nuceli of conscious, unrestrained rats: Possible mechanisms of action. Neuroscience 47:941-957; 1992.

4. Benarroch, E.E.; Balda, M.S.; Finkielman, S.; Nahmod, V.E. Neurogenic hypertension after depletion of norepinephrine in anterior hypothalamus induced by 6-hydroxydopamine administration into the ventral pons: Role of serotonin. Neuropharmacology 22:29-34; 1983.

5. Bhaskar, R.; Philip, L. Extracellular catechol and indole turnover in the nucleus of the solitary tract of Spontaneously Hypertensive and Wystar-Kyoto normotensive rats in repsonse to drug-induced changes in arterial blood pressure. Br. Res. Bull. 40:111-116; 1996.

6. Bhakskaran, O.; Freed, C.R. Changes in arterial blood pressure lead to baroreceptor-mediated changes in norepinephrin and 5-hydroxyindolacetic acid in rat nucleus tractus solitarius. J. Pharmacol. Exp. Ther. 245:356-363; 1988.

7. Brody, M.J.; Varner, K.J.; Vasquez, E.C.; Lewis, S.J. Central nervous system and the pathogenesis of hypertension: Sites and mechanisms. Hypertension 18(Suppl III):III-7-III-12; 1991.

8. Chen, Y.-F.; Meng, Q.-C.; Wyss, J.M.; Jin, H.-K.; Oparil,S. High NaCl diet reduces hypothalamic norepinephrine turnover in hypertensive rats. Hypertension 11:55-62; 1988.

9. Corder, R.; Castagne, V.; Rivet, J.M.; Mormede, P.; Gaillar, R.C. Central and peripheral effects of repeated stress and high NaCl diet on neuropeptide Y. Physiol. Behav. 52:205-210; 1992.

10. Cox, R.H.; Hubbard, J.W.; Lawler, J.E.; Sanders, B.J.; Mitchell, V.P. Exercise training attenuates stress-induced hypertension in the rat. Hypertension 7:745-751; 1985.

11. DeJong, W.; Zandberg, P.; Palkovits, M.; Bohus, B. Acute and chronic hypertension after lesions and transections of the rat brainstem. In: DeJong, W.; Provost, A.P.; Shapiro, A.P., eds. Progress in brain research vol 47: Hypertension and brain mechanisms. Amsterdam: Elsevier; 1977:189-197.

12. DiBona, G.F.; Jones, S.Y. Central alpha2-adrenoceptor responsiveness in borderline hypertensive rats. J. Hypertens. 9:543-547; 1991.

13. Doba, N.; Reis, D.J. Acute fulminating neurogenic hypertension produced by brainstem lesions in rat. Circ. Res. 32:584-593; 1973.

14. Ernsberger, P.; Azar, S.; Azar, P. The role of the anteromedial hypothalamus in Dahl hypertension. Brain Res. 15:451-454; 1985.

15. Folkow, B.; Nilsson, H. Transmitter release at adrenergic nerve endings: Total exocytosis or fractional release? News Physiol. Sci. 12:32-36; 1997.

16. Folkow, B.; Rubenstein, E.H. Cardiovascular effects of acute and chronic stimulation of the hypothalamic defense area in the rat. Acta Physiol. Scand. 68:48-57; 1966.

17. Forsyth, R.P.; Pesout, J. Cardiovascular effects of intracerebroventricular norepinephrin in consciuos and anaesthetized monkeys. Neuropharmacology 17:103-108; 1978.

18. Friedman, R.; Iwai, J. Dietary sodium, psychic stress, and genetic predisposition to experimental hypertension. Proc. Soc. Exp. Bio. Med. 155:449-452; 1977.

19. Glowinski, J.; Iversen, L.L. Regional studies of catecholamines in the rat brain-I: The disposition of [3-H]norepinephrine, [3-H]dopamine and [3-H]DOPA in various regions of the brain. J. Neurochem 13:655-669; 1966.

20. Hilton, S.M. Hypothalamic regulation of the cardiovascular system. Br. Med. Bull. 3:243-248; 1966.

21. Hilton, S.M.; Yardley, C.P. Blood pressure and heart rate- responses to long term stimulation of the hypothalamic defece area in the rat. J. Physiol. 373:85P; 1986.

22. Iwai, J.; Friedman, R.; Tassinari, L. Genetic influence on brain catecholamines: High brain noradrenaline in salt sensitive rats. Clin. Sci. 59:263s-265s; 1980.

23. Kawasaki, S.; Takeda, K.; Itoh, H; Takesako, T; Hirata, M.; Hayashi, J.; Oguro, M.; Nakamura, Y.; Sasaki, S.; Nakagawa, M. Altered noradrenergic projection to hypothalamus via baroreflex in spontaneously hypertensive rats. Am. J. Hypertens. 4:263-266; 1991.

24. Klangkalya, B; Spripairojthikoon, W.; Oparil, S.; Wyss, J.M. High NaCl diet increases anterior hypothalamic alpha sub(2)-adrenoceptors in SHR. Brain Res. 415:77-84; 1988.

25. Kraft, K.; Diehl, J.; Stumpe, K.O. Influence of chronic opioid delta receptor antagonism on blood pressure development. Clin. Exper. Hyper.-Theory Prac. A13:467-477; 1991.

26. Kventansky. R.; McCarty, R.; Thoa, N.B.; Lake, C.R.; Kopin, I.J. Sympatho-adrenal responses of spontaneously hypertensive rats to immobilization stress. Am. J. Physiol. 236:H457-H462; 1979.

27. Kventansky, R.; Palkovits, M.; Mitro, A.; Torda, T.; Mikulaj, L. Catecholamines in individual hypothalamic nuclei of acutely and repeatedly stressed rats. Neuroendocrinology 23:257-267; 1977.

28. Lawler, J.E.; Barker, G.F.; Hubbard, J.W.; Allen, M.T. The effect of conflict on tonic levels of blood pressure in the genetically borderline hypertensive rat. Psychophysiology 17:363-370; 1980.

29. Lawler, J.E.; Barker, G.F.; Hubbard, J.W.; Schaub, R.g. The effects of stress on blood pressure and cardiac pathology in rats with borderline hypertension. Hypertension 3:496-505; 1981.

30. Lawler, J.E.; Sanders, B.J.; Chen, Y.-F.; Nagahama, S.; Oparil, S. Hypertension produced by a high sodium diet in borderline hypertensive rat (BHR). Clin. Exp. Hypertens. A9:1713-1732; 1987.

31. Lawler, J.E.; Zheng, G.-P.; Li, S.-G.; Wang, C.-H.; Edgemon, I.P. Norepinephrine levels in discrete brain nuclei in borderline hypertensive rats exposed to compound stressors. Brain Res. Bull. 40:1-5; 1996.

32. Louis, W.J.; Conway, E.; Summers, R.; Beart, P.; Jarrott, B. Effects of methyldopa metabolites on amine transmitters and adrenergic receptors in rat brain. Hypertension 6(Suppl. II):II-40-II-44; 1984.

33. Marsden, C.A.; Routledge, C. Electrical stimulation of rat C1 neurones increases blood pressure and extracellular hypothalamic adrenaline. Br. J. Pharmacol. 86:415P; 1985.

34. Martin, J.R.; Beifeld, M.C.; Westfall, T.C. Blood pressure increases after injection of neuropeptide Y into posterior hypothalamic nucleus. Am. J. Physiol. 254:H879-H888; 1988.

35. Mermet, C.C.; Gonon, F.G. Ether stress stimulates noradrenaline release in the hypothalamic paraventricular nucleus. Neuroendocrinology 47:75-82; 1988.

36. Minson, J.B.; Chalmers, J.P.; Caon, A.C.; Renaud, B. Separate areas of rat medulla oblongata with populations of serotonin- and adrenaline-containing neurons alter blood pressure after *l*-glutamate stimulation. J. Auton. Nerv. Syst. 19:39-50; 1987.

37. Mitchell, V.P.; Lawler, J.E. Norepinephrine content of discrete brain nuclei in acutely and chronically stressed borederline hypertensive rats. Brain Res. Bull. 22:545-547; 1989.

38. Nakamura, K.; Nakamura, K. Activation of central noradrenrgic and adrenergic neurons in young and adult spontaneously hypertensive rats. Jpn. Heart J. 19:635-636; 1978.

39. Nakata, T.; Berard, W.; Kogosov, E.; Alexander, N. Cardiovascular change and hypothalamic norepinephrine release in response to environmental stress. Am. J. Physiol. 264:R784-R789; 1993.

40. Nakata, T.; Berard, W.; Kogosov, E.; Alexander, N. Hypothalamic NE release and cardiovascular response to NaCl in sinoaortic-denervated rats. Am. J. Physiol. 260:R733-R738; 1991.

41. Palkovits, M. Isolated removal of hypothalamic or other brain nuclei of the rat. Brain Res. 59:449-450; 1973.

42. Paxinos, G.; Watson, C. The rat brain in stereotaxic coordinates. New York: Academic Press; 1982.

43. Pawloski-Dahm, C.M.; Gordon, F.J. Increased dietary salt sensitizes vasomotor neurons of the rostral ventrolateral medulla. Hypertension 22:929-933; 1993.

44. Petty, M.A.; Reid, J.L. Changes in noradrenaline concentration in brain stem and hypothalamic nuclei during the development of renovascular hypertension. Br. Res. 136:376-380; 1977.

45. Quan-bui, K.; Elghozi, J.; Devnich, M.; Meyer, P. Early changes in NA content of some brain nuclei in the SHR. Clin. Sci. 59:243s-245s; 1980.

46. Routledge, C.; Marsden, C.A. Electrical stimulation of the C1 region of the rostral ventrolateral medualla of the rat increases mean arterial pressure and adrenaline release in the posterior hypothalamus. Neuroscience 20:457-466; 1987.

47. Saavedra, J.M. Brainstem adrenergic neurons participate in the regulation of the stress response and in genetic and experimental hypertension. In Fuxe, K., Goldstein, M., Hokfelt, B., Hokfelt, T. eds. Central adrenaline neurons: Basics aspects and their role in cardiovascular function. New York: Pergamon Press, 1980.

48. Saavedra, J.M.; Torda, T. Increased brain stem and decreased hypothalamic adrenaline-forming enzyme after acute and repeated immobilization stress in the rat. Neuroendocrinology 31:142-146; 1980.

49. Sanders, B.J.; Lawler, J.E. The borderline hypertensive rat (BHR) as a model for environmentally induced hypertension: A review and update. Neurosci. Biobehav. Rev. 16:207-217; 1992.

50. Smith, O.A.; Astley, C.A.; Devito, J.L.; Stein, J.M.; Walsh, K.E. Functional analysis of hypothalamic control of the cardiovascular responses accompanying emotional behavior. Fed. Proc. 39:2487-2494; 1980.

51. Tanaka, M.; Kohno, Y.; Nakagawa, R.; Ida, Y.; Takeda, S.; Nagasaki, N.; Noda, Y. Regional characteristics of stress-induced increases in brain noradrenaline release in rats. Pharmacol. Biochem. Behav. 19:543-547; 1983.

52. Tanaka, M.; Tsuda, A.; Yokoo, H.; Yoshida, M.; Ida, Y.; Nishimura, H. Involvement of the brain noradrenaline system in emotional changes caused by stress in rats. Ann. NY Acad. Sci. 597:159-174; 1990.

53. Uchida, T.; O'Brien, R.D. The effects of hydrazines on rat brain serotonin, norepinephrine, and gamma amino butyric acid. Biochem. Pharmacol. 13:725-730; 1964.

54. Wijen, H.J.L.M.; Spierenburg, H.A.; De Kloet, E.R.; DeJong, W.; Versteeg, D.H.G. Decrease in noradrenergic activity in hypothalamic nuclei during the development of spontaneous hypertension. Brain Res. 184:153-162; 1980.

55. Winternitz, S.R.; Katholi, R.E.; Oparil, S. Decrease in hypothalamic norepinephrine content following renal denervation in the one-kidney, one clip Goldblatt hypertensive rat. Hypertension 4:369-373; 1982.

56. Wintetnitz, S.R.; Oparil, S. Sodium-neural interactions in the development of spontaneous hypertension. Clin. Exp. Hypertens. A4:751-760; 1982.

57. Winternitz, S.R.; Wyss, J.M.; Meadows, J.R.; Oparil, S. Increased noradrenaline content of hypothalamic nuclei in association with worsening hypertension after high sodium intake in the young spontaneous hypertensive rat. Clin. Sci. 63:339s-342s; 1982.

58. Yardley, C.P.; Andrate, J.M.; Weaver, L.C. Evaluation of cardiovascular control by neurons in the dorsal medulla of rats. J. Auton, Nerv. Syst. 29:1-12; 1989.

59. Yokoo, H.; Tanaka, M.; Tanaka, T.; Tsuda, A. Stress-induced increase in noradrenaline release in the rat hypothalamus assessed by intracranial microdialysis. Experentia 46:290-292; 1990.

60. Zanchetti, A. Neural factors and catecholamines in experimental hypertension. In A. Zanchetti, ed. Neural and psychological mechanisms in cardiovascular disease. Milan: Casa Editrice; 1972:15-31.

Appendix

Table 1. Comparisons of means for BHR discrete nuclei during the varying durations of salt diet.

	A2	A1	C1	LC
Control vs .5 wks	18+/-8 / 13+/-3	9+/-2 / 14+/-1+	5+/-.6 / 13+/-1**	4+/-1 / 5+/-1
Control vs 1 wk	18+/-8 / 10+/-2	9+/-2 / 9+/-.9	5+/-.6 / 11+/-1**	4+/-1 / 3+/-.7
Control vs 2 wk	18+/-8 / 50+/-13+	9+/-2 / 24+/-7*	5+/-.6 / 10+/-1**	4+/-1 / 5+/-1
Control vs 4 wk	18+/-8 / 45+/-9+	9+/-2 / 19+/-2**	5+/-.6 / 12+/-1**	4+/-1 / 5+/-.6
Control vs 8 wk	18+/-8 / 13+/-7	9+/-2 / 9+/-2	5+/-.6 / 10+/-2*	4+/-1 / 3+/-1
.5 wk vs 1 wk	13+/-3 / 10+/-2	14+/-1 / 9+/-.9	13+/-1 / 11+/-1	5+/-1 / 3+/-.7+
.5 wk vs 2 wk	13+/-3 / 50+/-13*	14+/-1 / 24+/-7	13+/-1 / 10+/-1+	5+/-1 / 5+/-1
.5 wk vs 4 wk	13+/-3 / 45+/-9*	14+/-1 / 19+/-2*	13+/-1 / 12+/-1	5+/-1 / 5+/-.6
.5 wk vs 8 wk	13+/-3 / 13+/-7	14+/-1 / 9+/-2*	13+/-1 / 10+/-2	5+/-1 / 3+/-1
1 wk vs 2 wk	10+/-2 / 50+/-13**	9+/-.9 / 24+/-7*	11+/-1 / 10+/-1	3+/-.7 / 5+/-1
1 wk vs 4 wk	10+/-2 / 45+/-9**	9+/-.9 / 19+/-2**	11+/-1 / 12+/-1	3+/-.7 / 5+/-.6*
1 wk vs 8 wk	10+/-2 / 13+/-7	9+/-.9 / 9+/-2	11+/-1 / 10+/-2	3+/-.7 / 3+/-1
2 wk vs 4 wk	50+/-13 / 45+/-9	24+/-7 / 19 +/-2	10+/-1 / 12+/-1	5+/-1 / 5+/-.6
2 wk vs 8 wk	50+/-13 / 13+/-7+	24+/-7 / 9+/-2*	10+/-1 / 10+/-2	5+/-1 / 3+/-1
4 wk vs 8 wk	45+/-9 / 13+/-7+	19+/-2 / 9+/-2**	12+/-1 / 10+/-2	5+/-.6 / 3+/-1+
	PH	Arc	DMH	LH
Control vs .5 wk	8+/-1 / 48+/-6**	10+/-2 / 48+/-10**	28+/-5 / 71+/-10**	16+/-4 / 31+/-3**

Control vs 1 wk	8+/-1 / 36+/-8 **	10+/-2 / 27+/-7*	28+/-5 / 65+/-11*	16+/-4 / 25+/-4
Control vs 2 wk	8+/-1 / 92+/-28*	10+/-2 / 37+/-13**	28+/-5 / 50+/-2**	16+/-4 / 27+/-8*
Control vs 4 wk	8+/-1 / 61+/-11**	10+/-2 / 42+/-11**	28+/-5 / 66+/-8**	16+/-4 / 30+/-4*
Control vs 8 wk	8+/-1 / 14+/-3+	10+/-2 / 10+/-1	28+/-5 / 37+/-9	16+/-4 / 22+/-3
.5 wk vs 1 wk	48+/-6 / 36+/-8	48+/-10 / 27+/-7	71+/-10 / 65+/-11	31+/-3 / 25+/-4
.5 wk vs 2 wk	48+/-6 / 92+/-28*	48+/-10 / 37+/-13	71+/-10 / 50+/-2	31+/-3 / 27+/-8
.5 wk vs 4 wk	48+/-6 / 61+/-11	48+/-10 / 42+/-11	71+/-10 / 66+/-8	31+/-3 / 30+/-4
.5 wk vs 8 wk	48+/-6 / 14+/-3**	48+/-10 / 10+/-1*	71+/-10 / 37+/-9**	31+/-3 / 22+/-3+
1 wk vs 2 wk	36+/-8 / 92+/-28*	27+/-7 / 37+/-13	65+/-11 / 50+/-2	25+/-4 / 27+/-8
1 wk vs 4 wk	36+/-8 / 61+/-11+	27+/-7 / 42+/-11	65+/-11 / 66+/-8	25+/-4 / 30+/-4
1 wk vs 8 wk	36+/-8 / 14+/-3*	27+/-7 / 10+/-1*	65+/-11 / 37+/-9+	25+/-4 / 22+/-3
2 wk vs 4 wk	92+/-28 / 61+/-11	37+/-13 / 42+/-11	50+/-2 / 66+/-8	27+/-8 / 30+/-4
2 wk vs 8 wk	92+/-28 / 14+/-3**	37+/-13 / 10+/-1**	50+/-2 / 37+/-9	27+/-8 / 22+/-3+
4 wk vs 8 wk	61+/-11 / 14+/-3**	42+/-11 / 10+/-1**	66+/-8 / 37+/-9*	30+/-4 / 22+/-3+

	VMH	PVH	Ant	SO
Control vs .5 wk	13+/-3 / 59+/-12**	20+/-4 / 78+/-12**	18+/-4 / 44+/-4**	9+/-2 / 36+/-5**
Control vs 1 wk	13+/-3 / 64+/-7**	20+/-4 / 70+/-6**	18+/-4 / 39+/-4**	9+/-2 / 30+/-5**
Control vs 2 wk	13+/-3 / 42+/-4*	20+/-4 / 52+/-10**	18+/-4 / 35+/-4*	9+/-2 / 54+/-15**
Control vs 4 wk	13+/-3 / 58+/-8**	20+/-4 / 89+/-11**	18+/-4 / 36+/-3**	9+/-2 / 46+/-6**
Control vs 8 wk	13+/-3 / 27+/-7	20+/-4 / 24+/-5	18+/-4 / 30+/-6	9+/-2 / 15+/-3+
.5 wk vs 1 wk	59+/-12 / 64+/-7	78+/-12 / 70+/-6	44+/-4 / 39+/-4	36+/-5 / 30+/-5
.5 wk vs 2 wk	59+/-12 / 42+/-4	78+/-12 / 52+/-10	44+/-1 / 35+/-4	36+/-5 / 54+/-15
.5 wk vs 4 wk	59+/-12 / 58+/-8	78+/-12 / 89+/-11	44+/-1 / 36+/-3	36+/-5 / 46+/-6
.5 wk vs 8 wk	59+/-12 / 27+/-7*	78+/-12 / 24+/-5**	44+/-1 / 30+/-6*	36+/-5 / 15+/-3**
1 wk vs 2 wk	64+/-7 / 42+/-4*	70+/-6 / 52+/-10	39+/-4 / 35+/-4	30+/-5 / 54+/-15+
1 wk vs 4 wk	64+/-7 / 58+/-8	70+/-6 / 89+/-11	39+/-4 / 36+/-3	30+/-5 / 46+/-6+
1 wk vs 8 wk	64+/-7 / 27+/-7**	70+/-6 / 24+/-5**	39+/-4 / 30+/-6+	30+/-5 / 15+/-3*

2 wk vs 4 wk	42+/-4 / 58+/-8	52+/-10 / 89+/-11*	35+/-4 / 36+/-3	54+/-15 / 46+/-6
2 wk vs 8 wk	42+/-4 / 27+/-7+	25+/-10 / 24+/-5*	35+/-4 / 30+/-6	54+/-15 / 15+/-3**
4 wk vs 8 wk	58+/-8 / 27+/-7**	89+/-11 / 24+/-5**	36+/-3 / 30+/-6	46+/-4 / 15+/-3**

*+ signifies p<.1, * signifies p<.05, ** signifies p<.01*

Table 2. Comparisons of means for WKY discrete nuclei during the varying durations of salt diet.

	A2	A1	C1	LC
Control vs .5 wk	10+/-2 / 18+/-2*	8+/-2 / 19+/-2**	8+/-2 / 13+/-.9*	4+/-.7 / 5+/-2
Control vs 1 wk	10+/-2 / 18+/-3+	8+/-2 / 12+/-2	8+/-2 / 12+/-2	4+/-.7 / 0+/-0*
Control vs 2 wk	10+/-2 / 24+/-6	8+/-2 / 12+/-2	8+/-2 / 10+/-.7	4+/-.7 / 5+/-.7
Control vs 4 wk	10+/-2 / 22+/-5	8+/-2 / 15+/-1**	8+/-2 / 14+/-1*	4+/-.7 / 5+/-1
Control vs 8 wk	10+/-2 / 14+/-5	8+/-2 / 13+/-2+	8+/-2 / 9+/-.8	4+/-.7 / 6+/-1
.5 wk vs 1 wk	18+/-2 / 18+/-3	19+/-2 / 12+/-2**	13+/-.9 / 12+/-2	5+/-2 / 0+/-0
.5 wk vs 2 wk	18+/-2 / 24+/-6	19+/-2 / 12+/-2*	13+/-.9 / 10+/-.7**	5+/-2 / 5+/-.7
.5 wk vs 4 wk	18+/-2 / 22+/-5	19+/-2 / 15+/-1+	13+/-.9 / 14+/-1	5+/-2 / 5+/-1
.5 wk vs 8 wk	18+/-2 / 14+/-5	19+/-2 / 13+/-2*	13+/-.9 / 9+/-.8**	5+/-2 / 6+/-1
1 wk vs 2 wk	18+/-3 / 24+/-6	12+/-2 / 12+/-2	12+/-2 / 10+/-.7	0+/-0 / 5+/-.7**
1 wk vs 4 wk	18+/-3 / 22+/-5	12+/-2 / 15+/-1	12+/-2 / 14+/-1	0+/-0 / 5+/-1+
1 wk vs 8 wk	18+/-3 / 14+/-5	12+/-2 / 13+/-2	12+/-2 / 9+/-.8	0+/-0 / 6+/-1+
2 wk vs 4 wk	24+/-6 / 22+/-5	12+/-2 / 15+/-1	10+/-.7 / 14+/-1**	5+/-.7 / 5+/-1
2 wk vs 8 wk	24+/-6 / 14+/-5	12+/-2 / 13+/-2	10+/-.7 / 9+/-.8	5+/-.7 / 6+/-1
4 wk vs 8 wk	22+/-5 / 14+/-5	15+/-1 / 13+/-2	14+/-1 / 9+/-.8**	5+/-1 / 6+/-1
	PH	Arc	DMH	LH
Control vs .5 wk	30+/-7 / 66+/-11*	19+/-11 / 44+/-12	38+/-10 / 104+/-14**	19+/-4 / 44+/-6**
Control vs 1 wk	30+/-7 / 47+/-7	19+/-11 / 47+/-14	38+/-10 / 64+/-8*	19+/-4 / 36+/-6*
Control vs 2 wk	30+/-7 / 44+/-7	19+/-11 / 31+/-7	38+/-10 / 56+/-10	19+/-4 / 24+/-4
Control vs 4 wk	30+/-7 / 53+/-10	19+/-11 / 55+/-8*	38+/-10 / 70+/-9*	19+/-4 / 34+/-3*
Control vs 8 wk	30+/-7 / 44+/-10	19+/-11 / 36+/-7	38+/-10 / 60+/-11	19+/-4 / 31+/-4+

.5 wk vs 1 wk	66+/-11 / 47+/-7	44+/-12 / 47+/-14	104+/-14 / 64+/-8*	44+/-6 / 36+/-6
.5 wk vs 2 wk	66+/-11 / 44+/-7*	44+/-12 / 31+/-7	104+/-14 / 56+/-10*	44+/-6 / 24+/-4**
.5 wk vs 4 wk	66+/-11 / 53+/-10	44+/-12 / 55+/-8	104+/-10 / 70+/-9*	44+/-6 / 34+/-3+
.5 wk vs 8 wk	66+/-11 / 44+/-10	44+/-12 / 36+/-7	104+/-40 / 60+/-11*	44+/-6 / 31+/-4+
1 wk vs 2 wk	47+/-7 / 44+/-7	47+/-14 / 31+/-7	64+/-8 / 56+/-10	36+/-6 / 24+/-4+
1 wk vs 4 wk	47+/-7 / 53+/-10	47+/-14 / 55+/-8	64+/-8 / 70+/-9	36+/-6 / 34+/-3
1 wk vs 8 wk	47+/-7 / 44+/-10	47+/-14 / 36+/-7	64+/-8 / 60+/-11	36+/-6 / 31+/-4
2 wk vs 4 wk	44+/-7 / 53+/-10	31+/-7 / 55+/-8*	56+/-10 / 70+/-9	24+/-4 / 34+/-3+
2 wk vs 8 wk	44+/-7 / 44+/-10	31+/-7 / 36+/-7	56+/-10 / 60+/-11	24+/-4 / 31+/-3
4 wk vs 8 wk	53+/-10 / 44+/-10+	55+/-8 / 36+/-7	70+/-9 / 60+/-11	34+/-3 / 31+/-3
	VMH	PVH	Ant	SO
Control vs .5 wk	27+/-9 / 73+/-11**	24+/-8 / 99+/-11**	28+/-10 / 62+/-7*	13+/-10 / 43+/-6*
Control vs 1 wk	27+/-9 / 58+/-8*	24+/-8 / 81+/-12**	28+/-10 / 55+/-8*	13+/-10 / 41+/-8*
Control vs 2 wk	27+/-9 / 70+/-12*	24+/-8 / 54+/-7*	28+/-10 / 48+/-9	13+/-10 / 25+/-4
Control vs 4 wk	27+/-9 / 86+/-11**	24+/-8 / 78+/-10**	28+/-10 / 54+/-7*	13+/-10 / 39+/-4*
Control vs 8 wk	27+/-9 / 42+/-4	24+/-8 / 61+/-11*	28+/-10 / 36+/-7	13+/-10 / 43+/-7*
.5 wk vs 1 wk	73+/-11 / 58+/-8	99+/-11 / 81+/-12	62+/-7 / 55+/-8	43+/-6 / 41+/-8
.5 wk vs 2 wk	73+/-11 / 70+/-12	99+/-11 / 54+/-7**	62+/-7 / 48+/-9	43+/-6 / 25+/-4**
.5 wk vs 4 wk	73+/-11 / 86+/-11	99+/-11 / 78+/-10	62+/-7 / 54+/-7	43+/-6 / 39+/-4
.5 wk vs 8 wk	73+/-11 / 42+/-4*	99+/-11 / 61+/-11*	62+/-7 / 36+/-7*	43+/-6 / 43+/-7
1 wk vs 2 wk	58+/-8 / 70+/-12	81+/-12 / 54+/-7+	55+/-8 / 48+/-9	41+/-8 / 25+/-4+
1 wk vs 4 wk	58+/-8 / 86+/-11+	81+/-12 / 78+/-10	55+/-8 / 54+/-7	41+/-8 / 39+/-4
1 wk vs 8 wk	58+/-8 / 42+/-4+	81+/-12 / 61+/-11	55+/-8 / 36+/-7+	41+/-7 / 43+/-7
2 wk vs 4 wk	70+/-12 / 86+/-11	54+/-7 / 78+/-10+	48+/-9 / 54+/-7	25+/-4 / 39+/-4*
2 wk vs 8 wk	70+/-2 / 42+/-4+	54+/-7 / 61+/-11	48+/-9 / 36+/-7	25+/-4 / 43+/-7*
4 wk vs 8 wk	86+/-11 / 42+/-4**	78+/-10 / 61+/-11	54+/-7 / 36+/-7+	39+/-4 / 43+/-7

*+ signifies p<.1, * signifies p<.05, ** signifies p<.01*

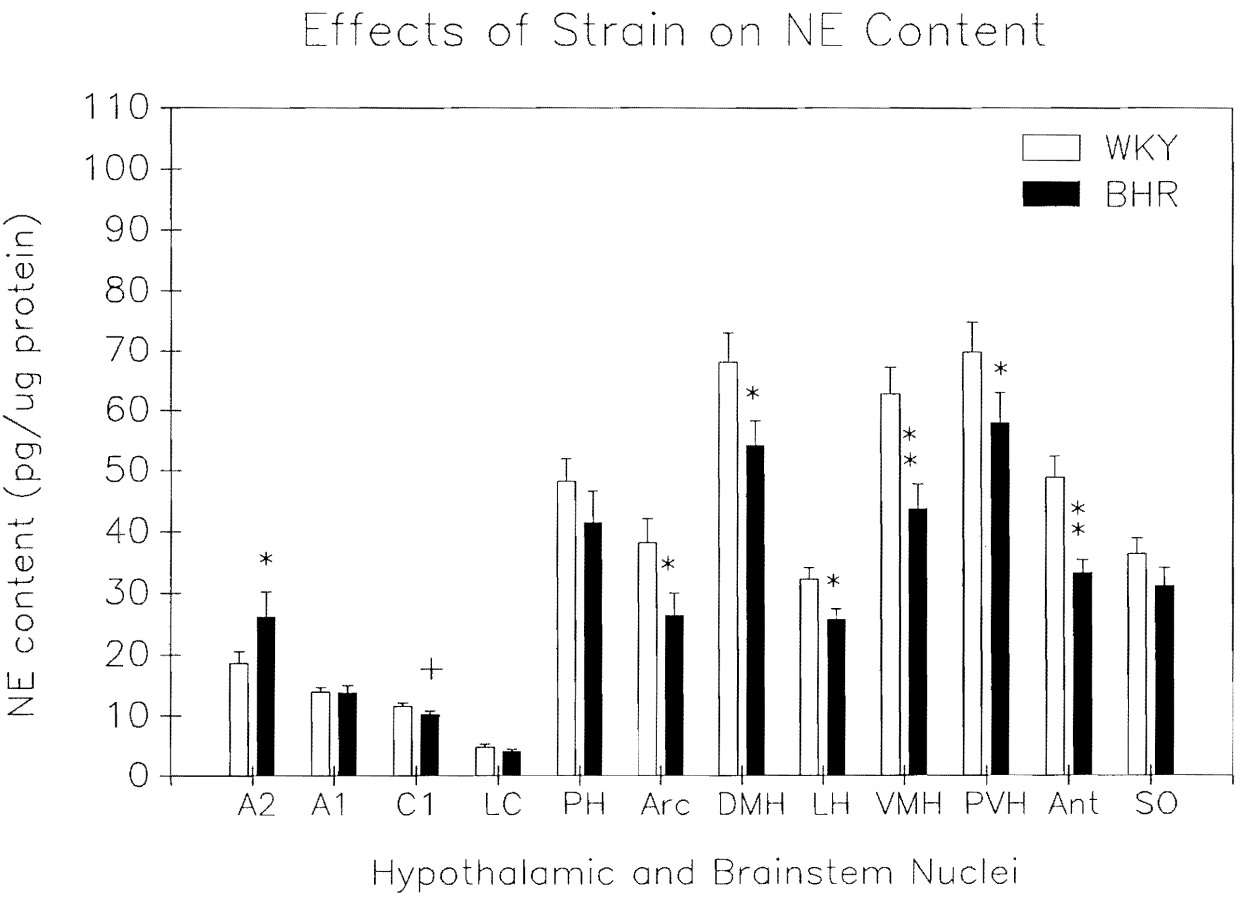

Figure 1. Mean (+/- SEM) NE concentrations for WKY and BHR across the high salt diet durations. (**p<.01, *p<.05, and +p<.10 for comparison between strains)

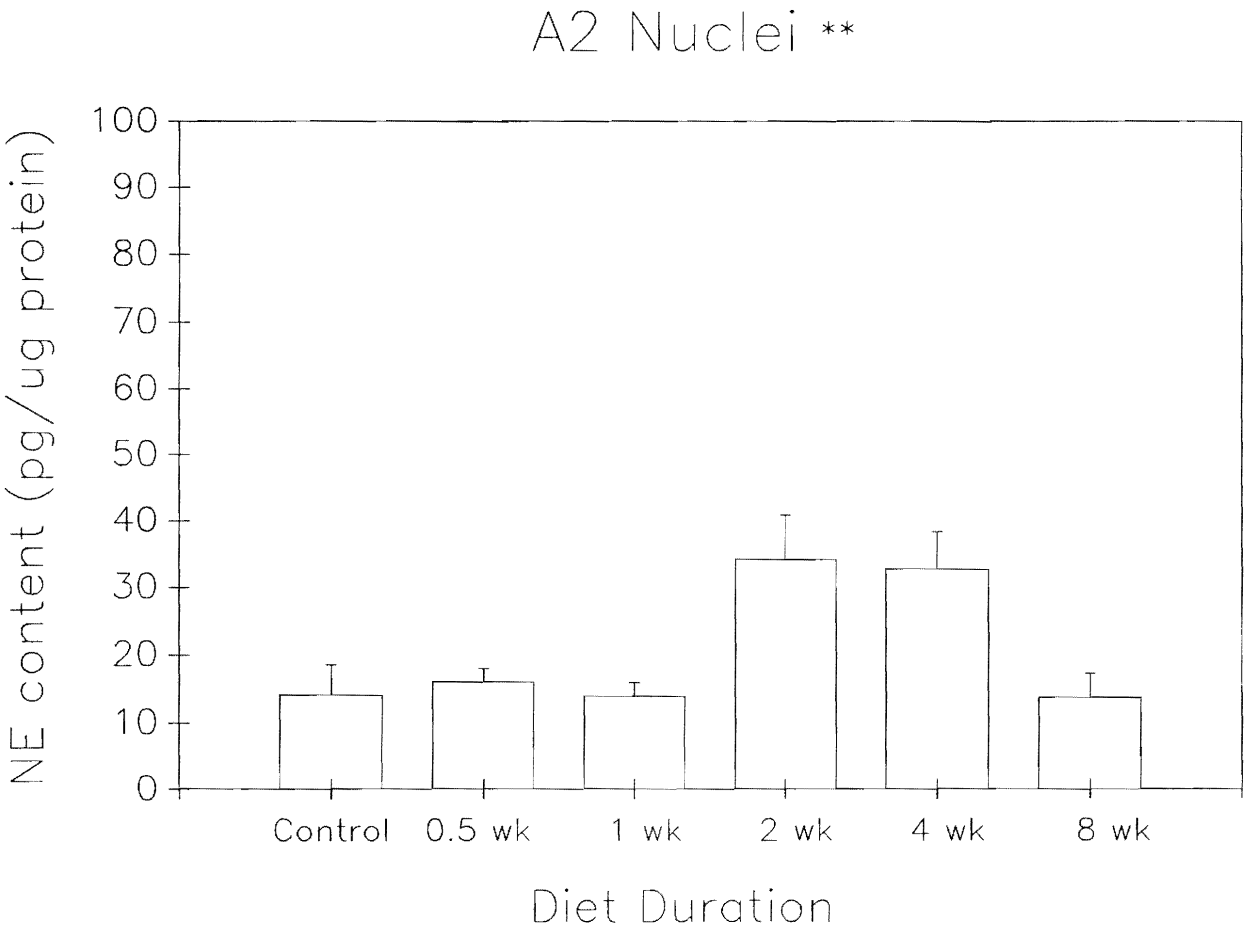

Figure 2. Mean (+/- SEM) NE concentrations in the A2 nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

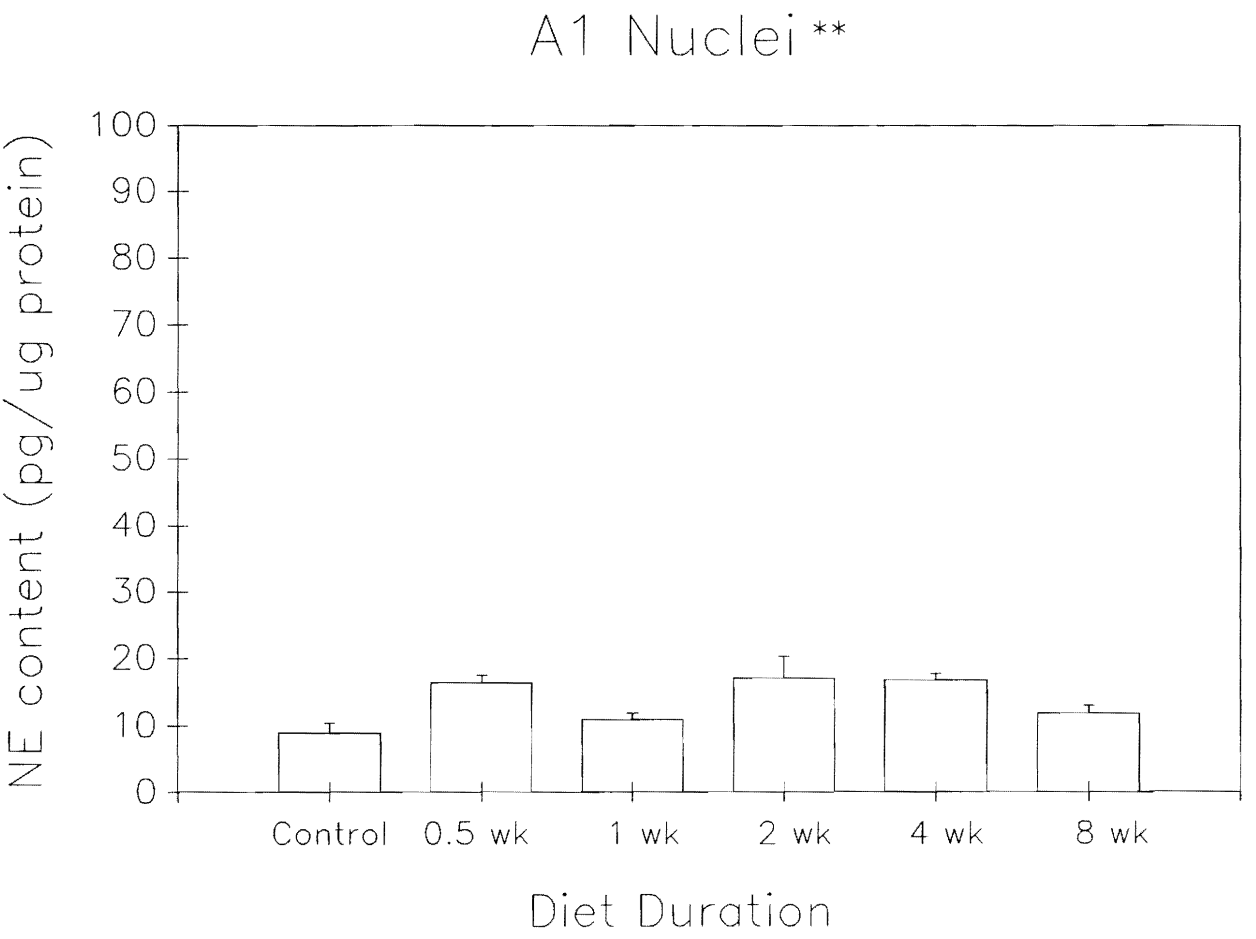

Figure 3. Mean (+/- SEM) NE concentrations in the A1 nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

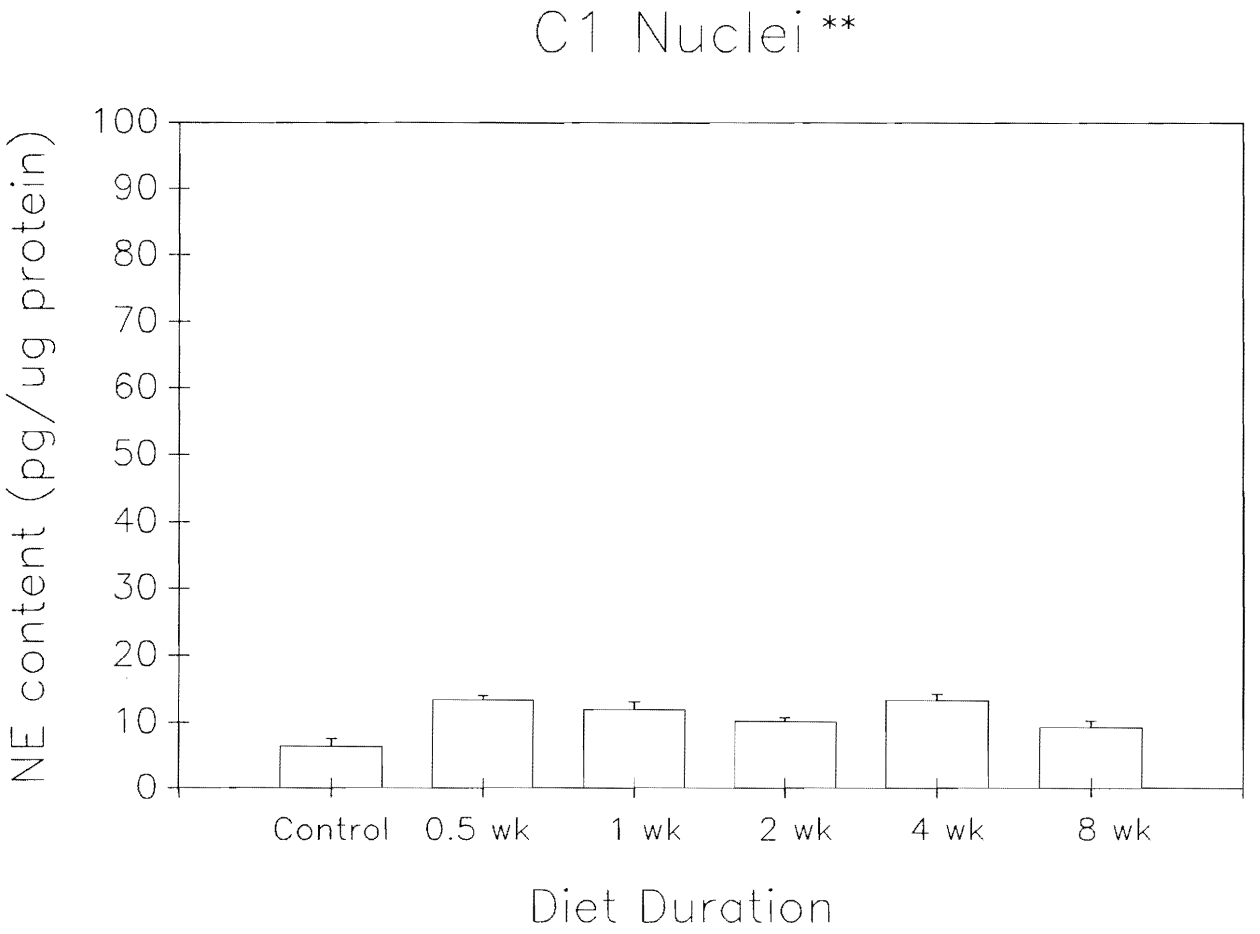

Figure 4. Mean (+/- SEM) NE concentrations in the C1 nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

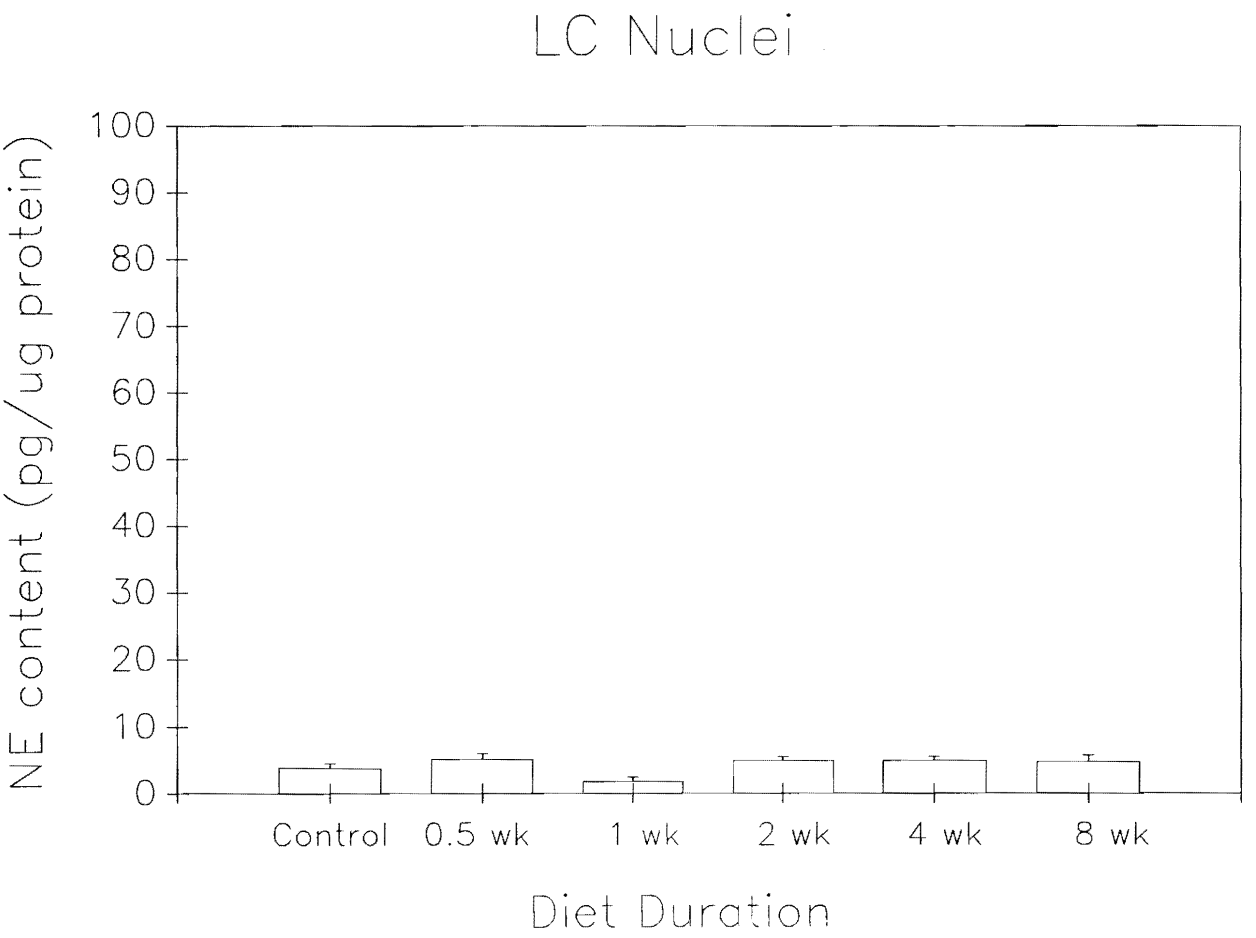

Figure 5. Mean (+/- SEM) NE concentrations in the LC nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR.

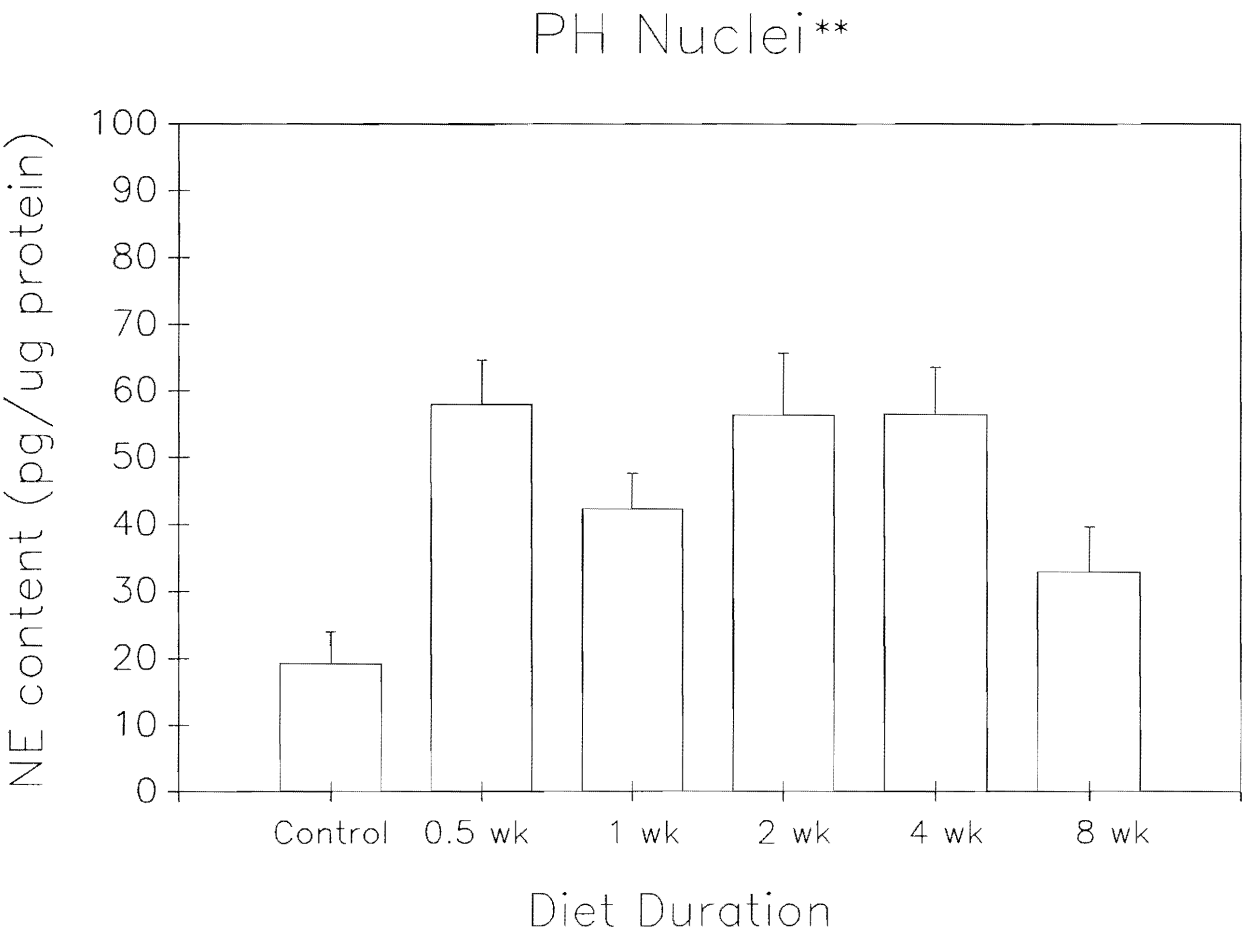

Figure 6. Mean (+/- SEM) NE concentrations in the PH nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

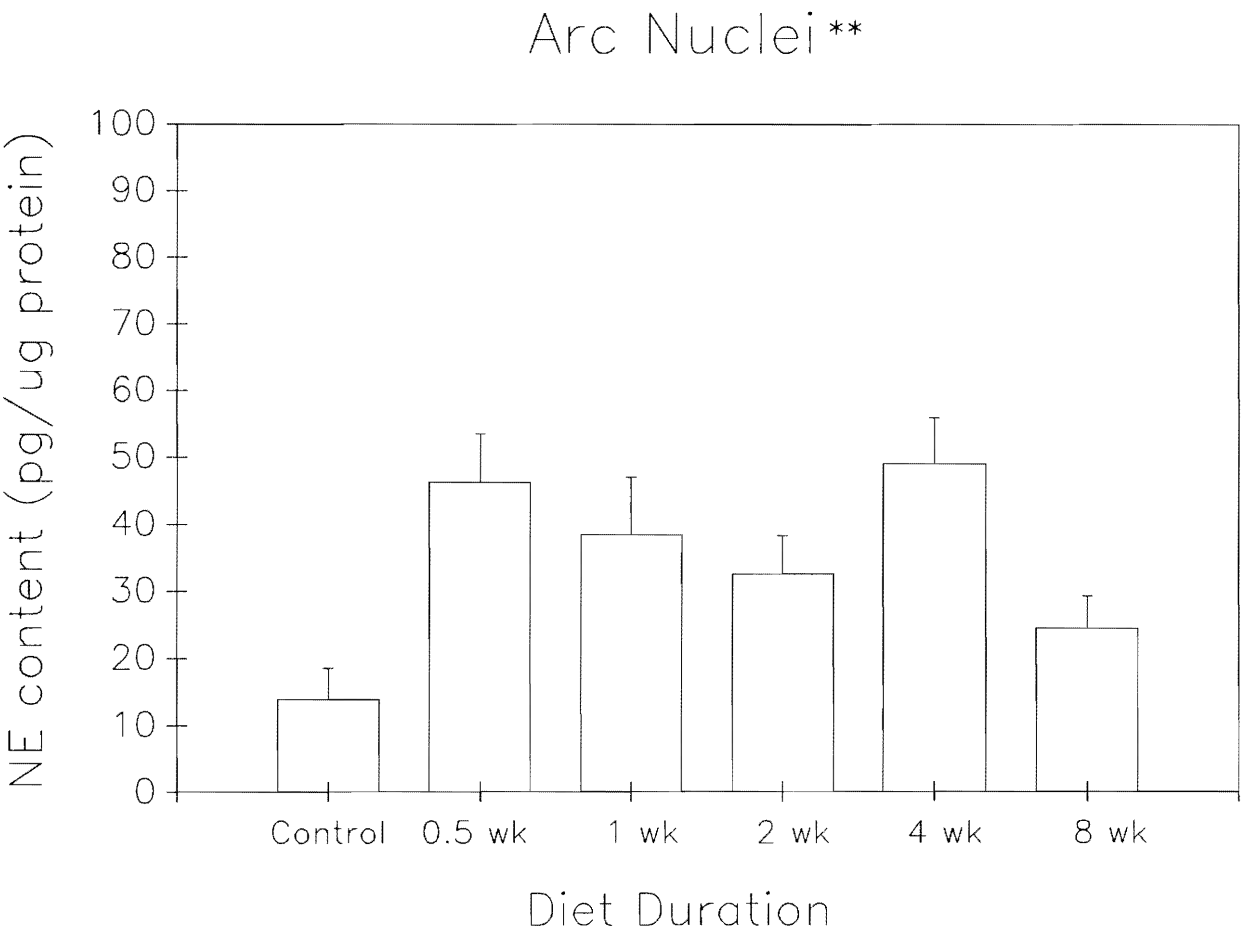

Figure 7. Mean (+/- SEM) NE concentrations in the Arc nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

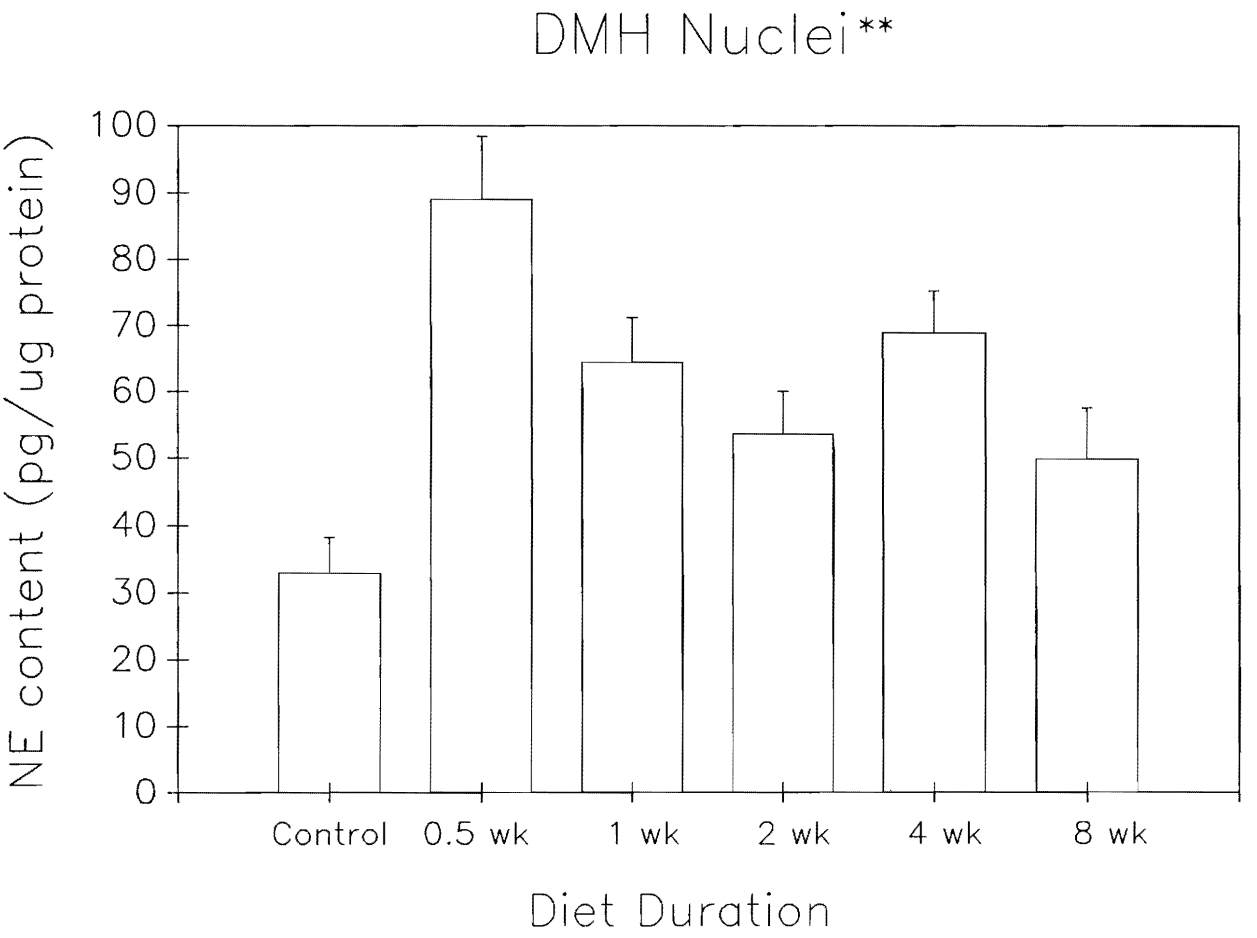

Figure 8. Mean (+/- SEM) NE concentrations in the DMH nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

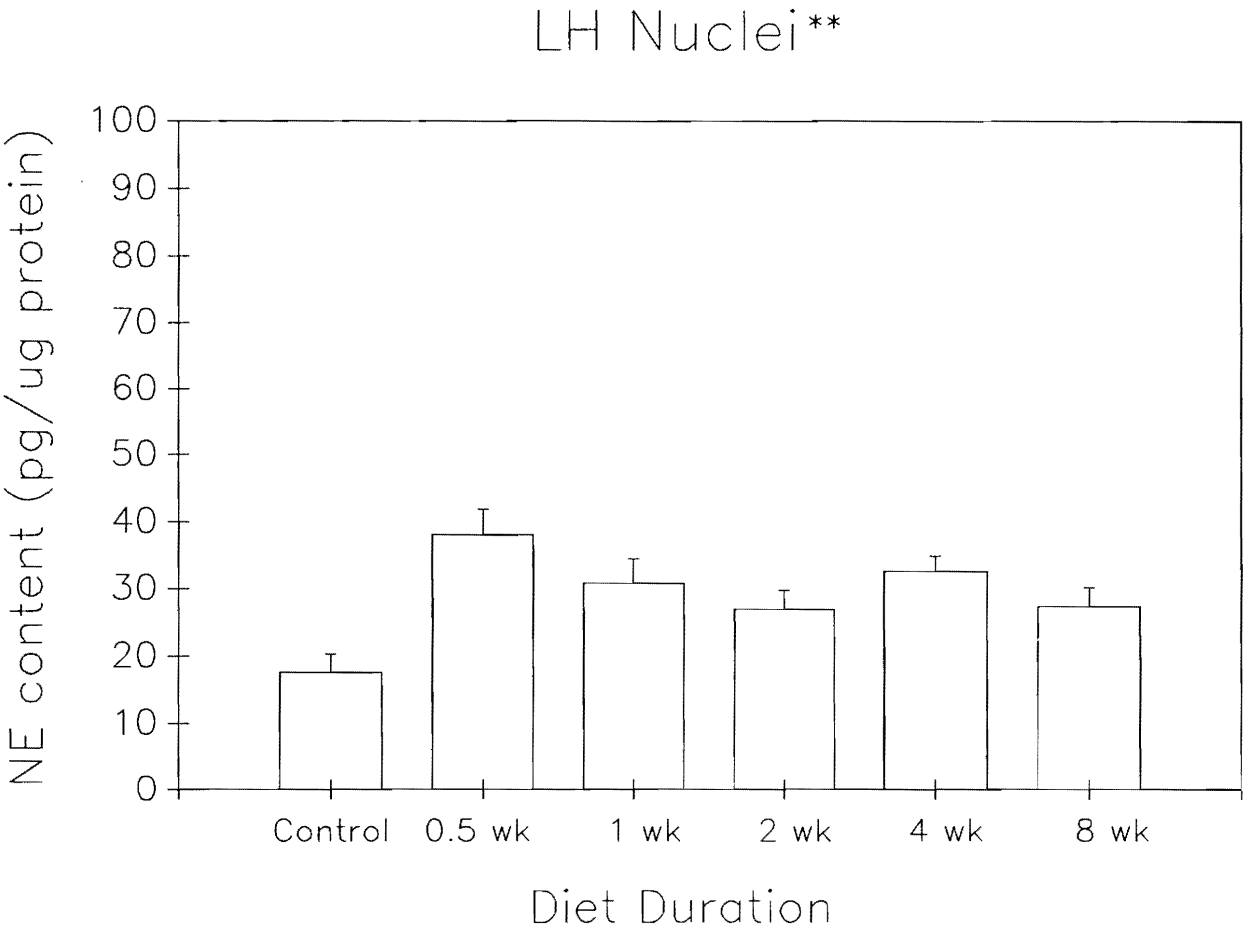

Figure 9. Mean (+/- SEM) NE concentrations in the LH nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

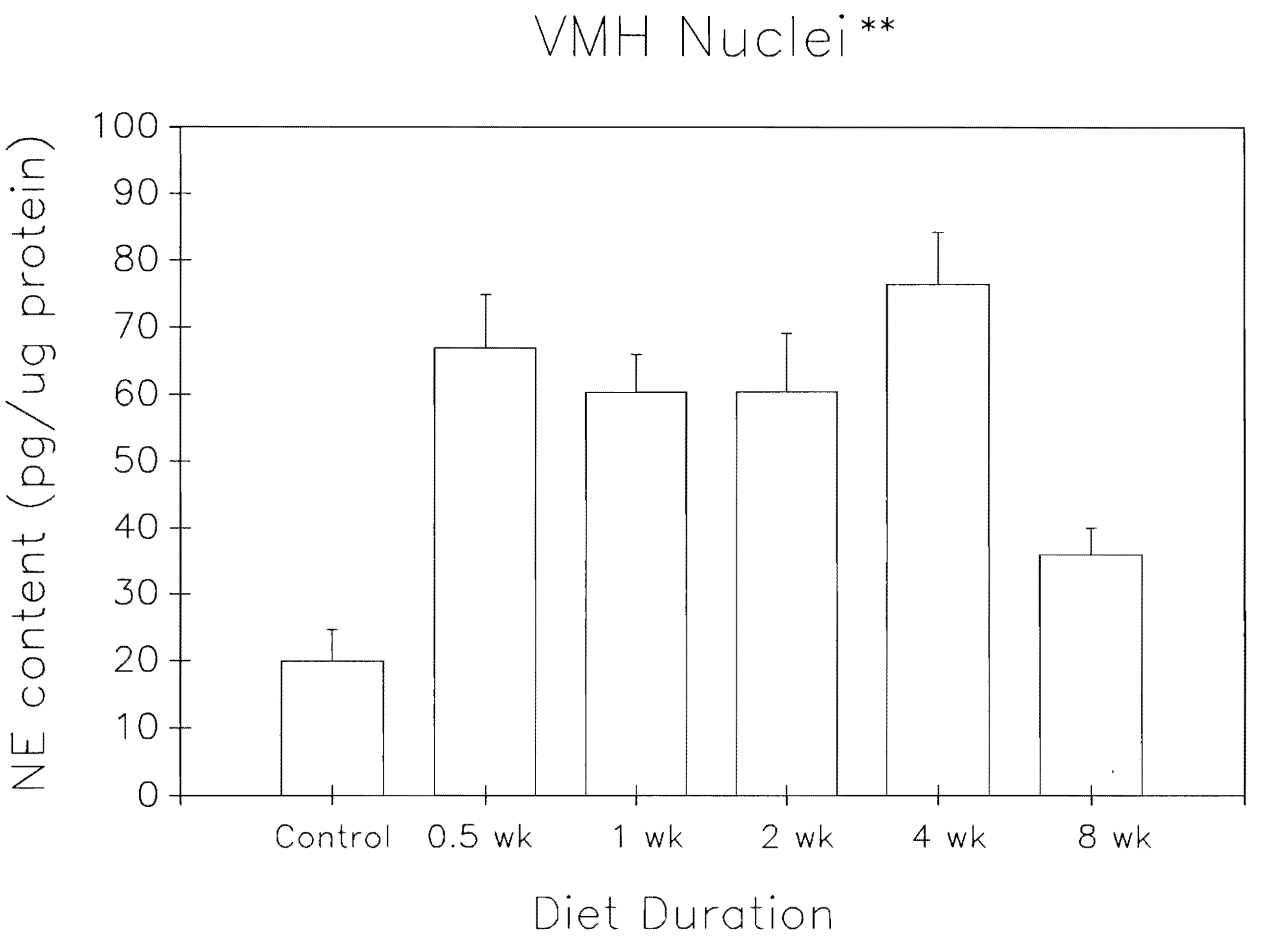

Figure 10. Mean (+/- SEM) NE concentrations in the VMH nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

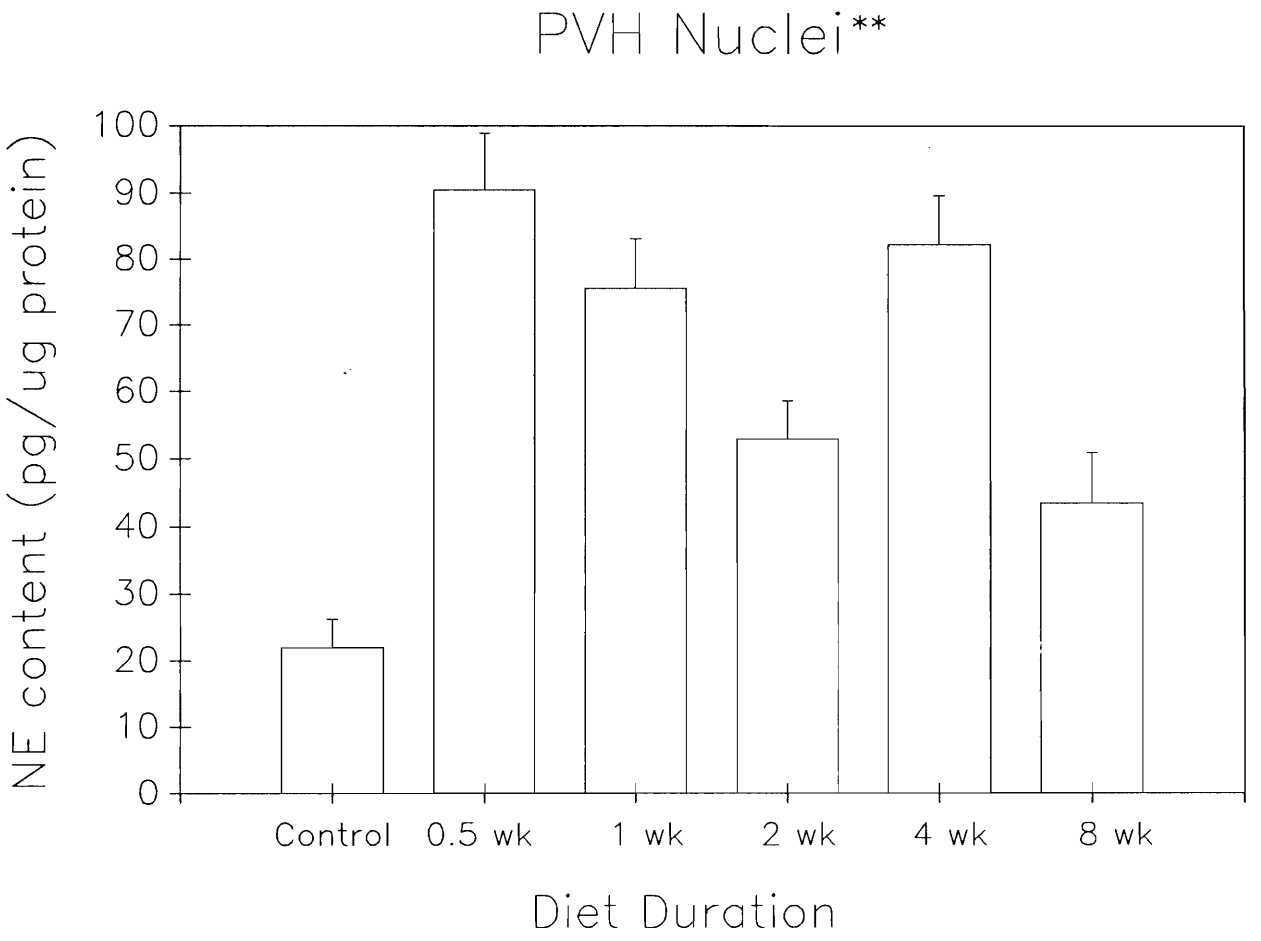

Figure 11. Mean (+/- SEM) NE concentrations in the PVH nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

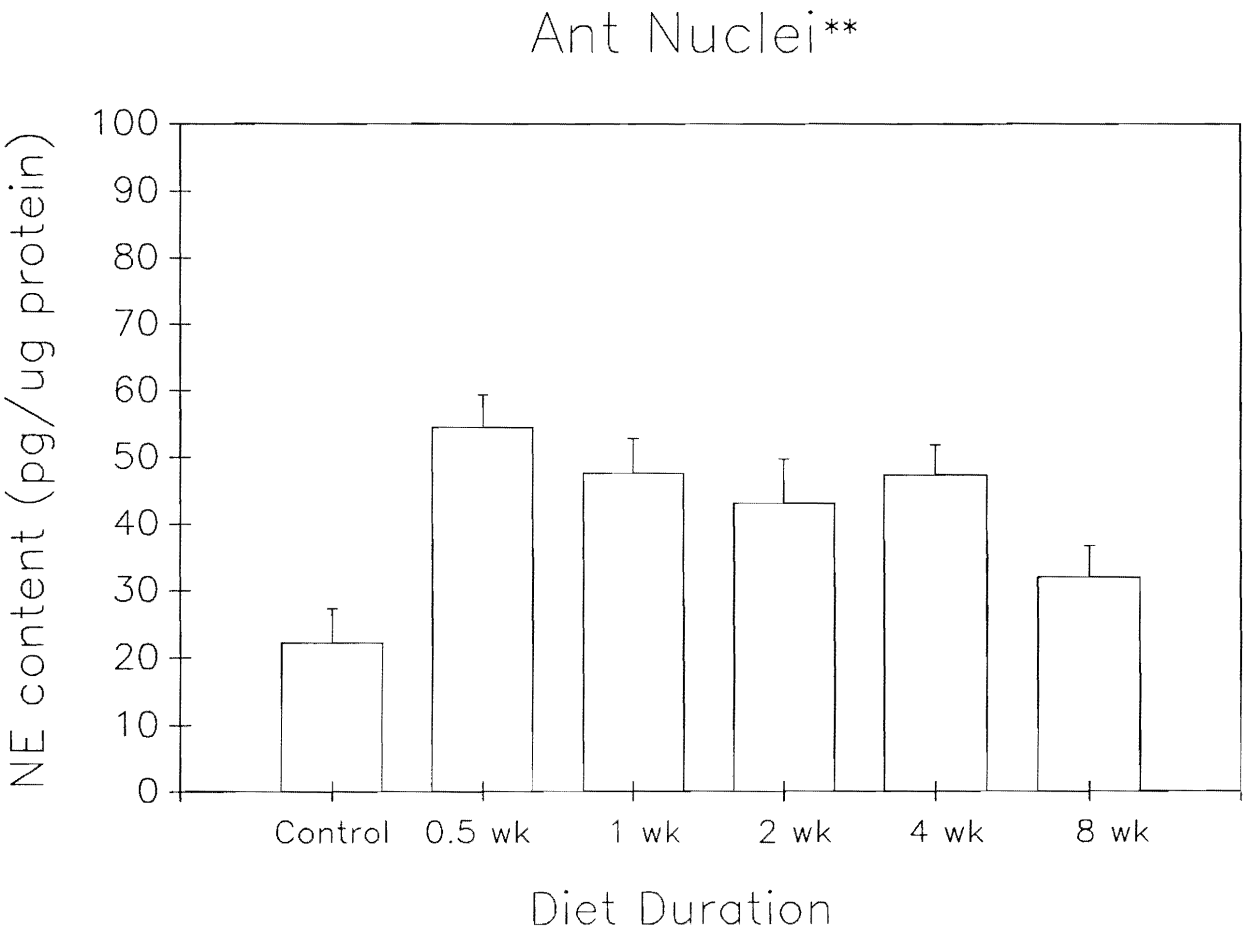

Figure 12. Mean (+/- SEM) NE concentrations in the Ant nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

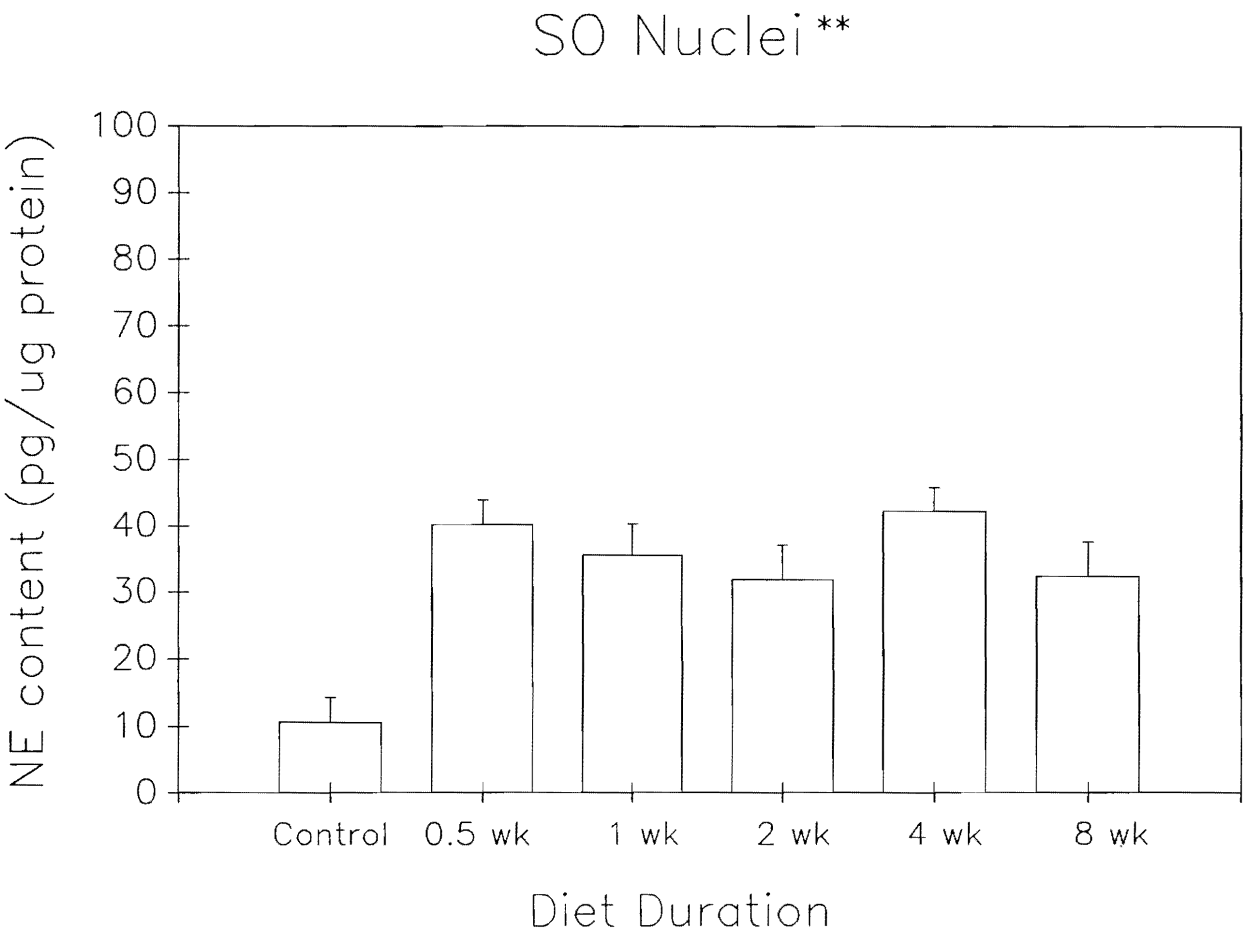

Figure 13. Mean (+/- SEM) NE concentrations in the SO nuclei for the control diet, .5, 1, 2, 4, and 8 week high salt diet collapsed over both WKY and BHR. (**p<.01 for comparison between durations)

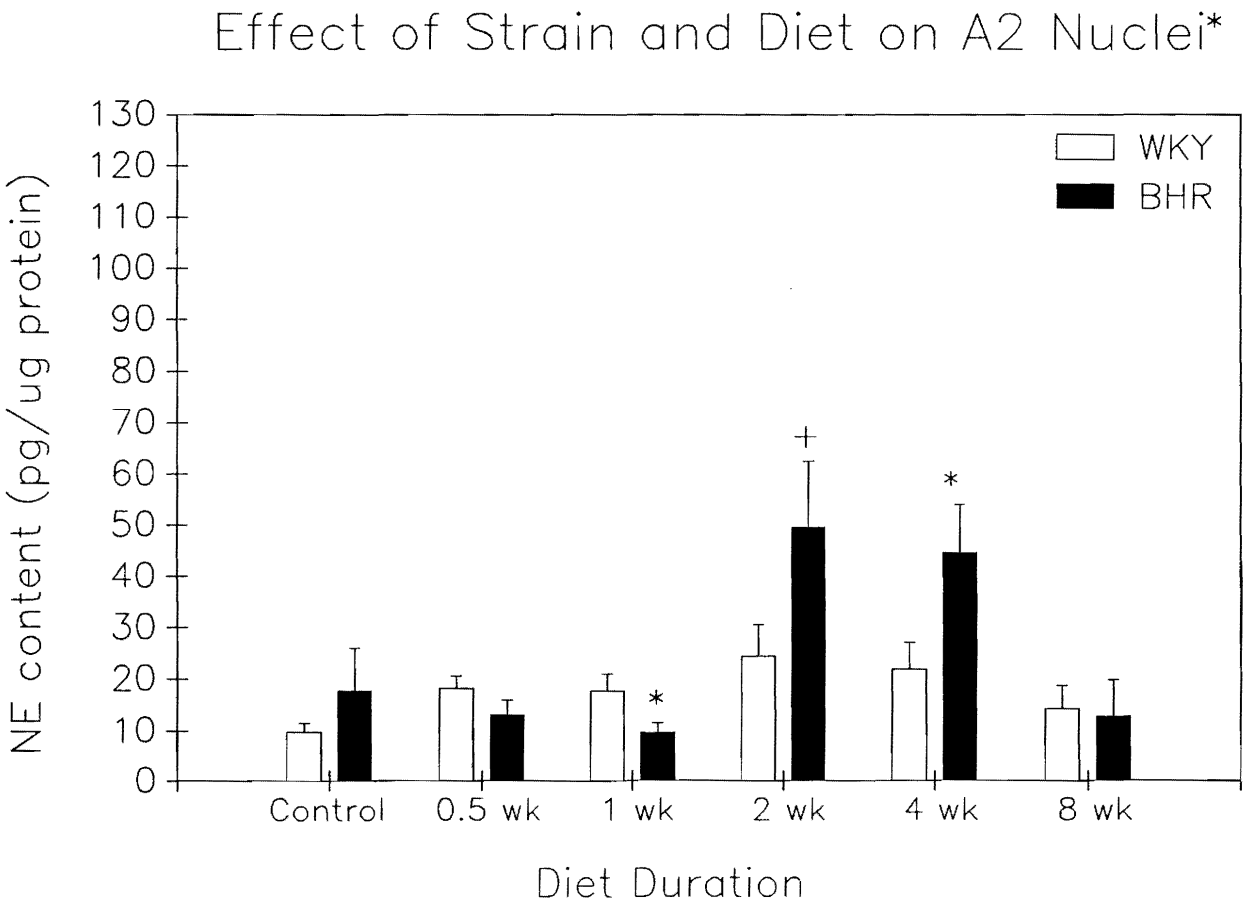

Figure 14. Mean (+/- SEM) NE concentrations of A2 nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (*p<.05 and +p<.10 for comparisons between strains and *p<.05 for strain-diet interaction)

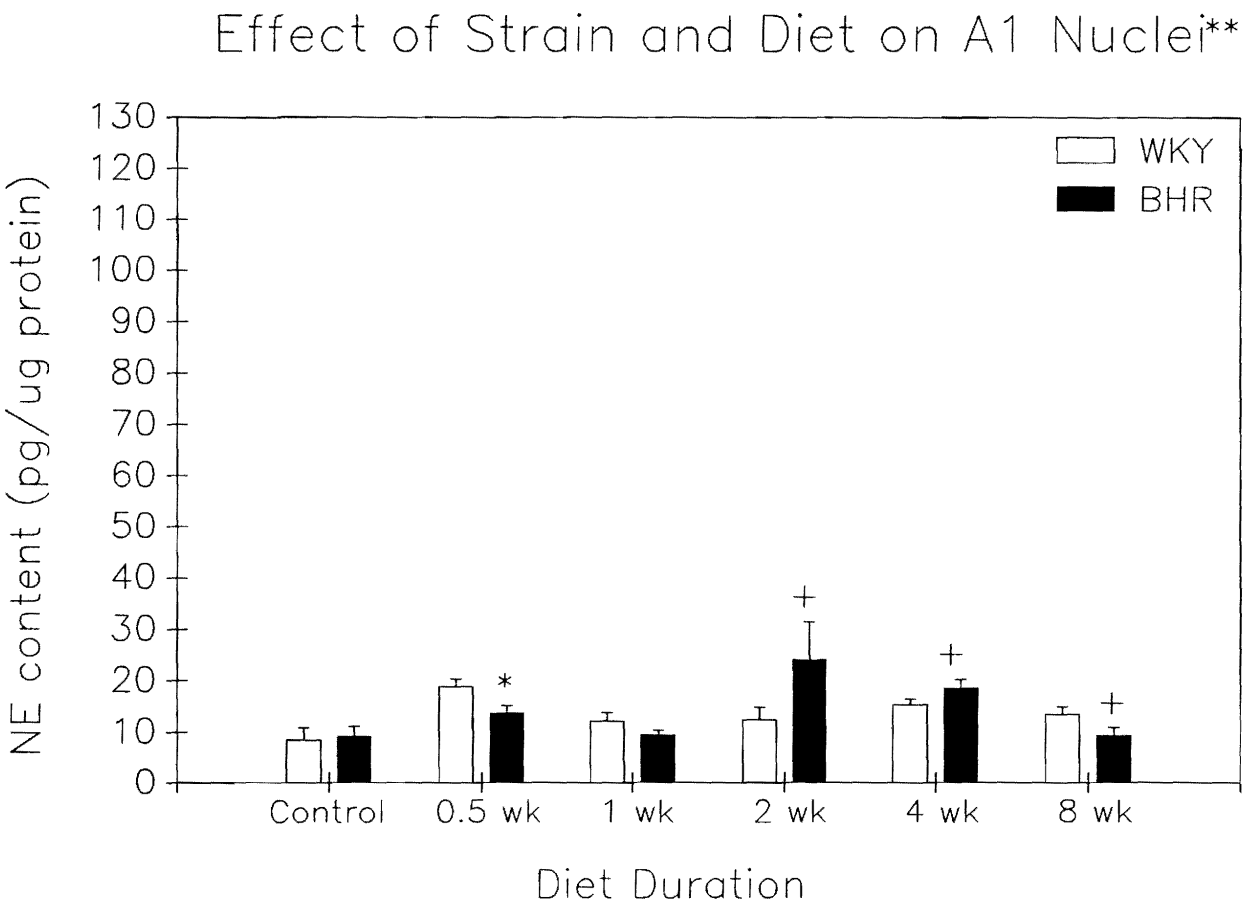

Figure 15. Mean (+/- SEM) NE concentrations of A1 nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (**p<.01, *p<.05 and +p<.10 for comparisons between strains and **p<.01 for strain-diet interaction)

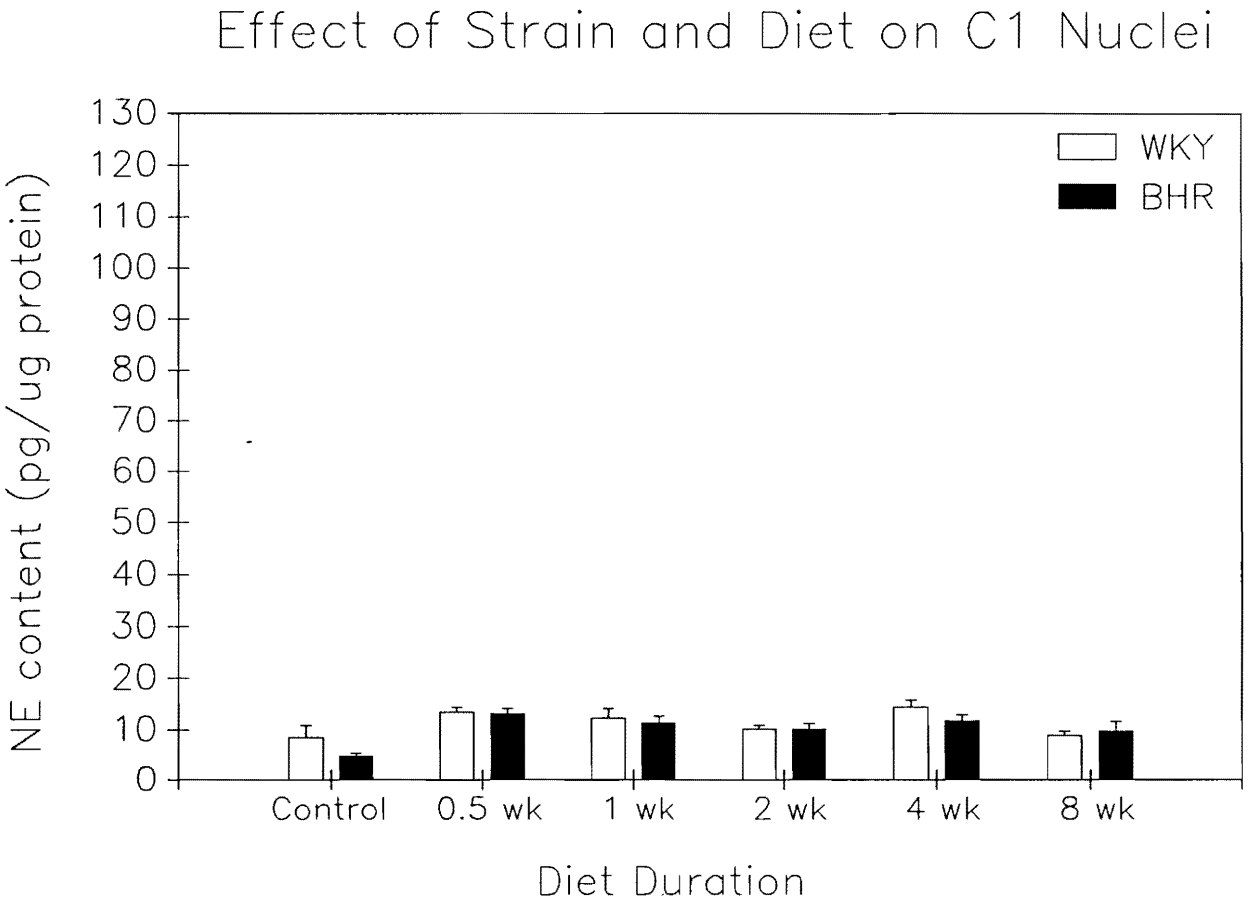

Figure 16. Mean (+/- SEM) NE concentrations of C1 nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets.

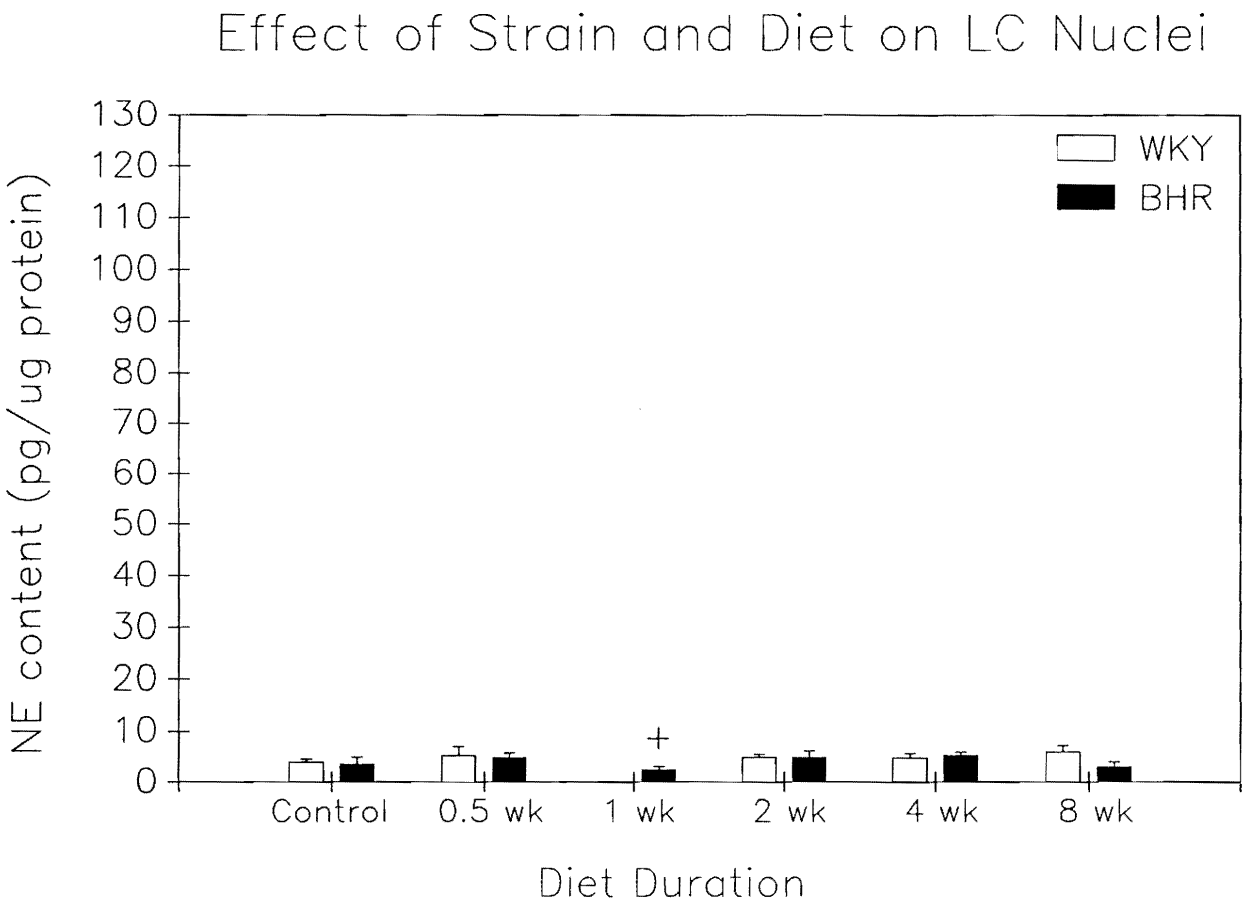

Figure 17. Mean (+/- SEM) NE concentrations of LC nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (+$p<.10$ for comparisons between strains)

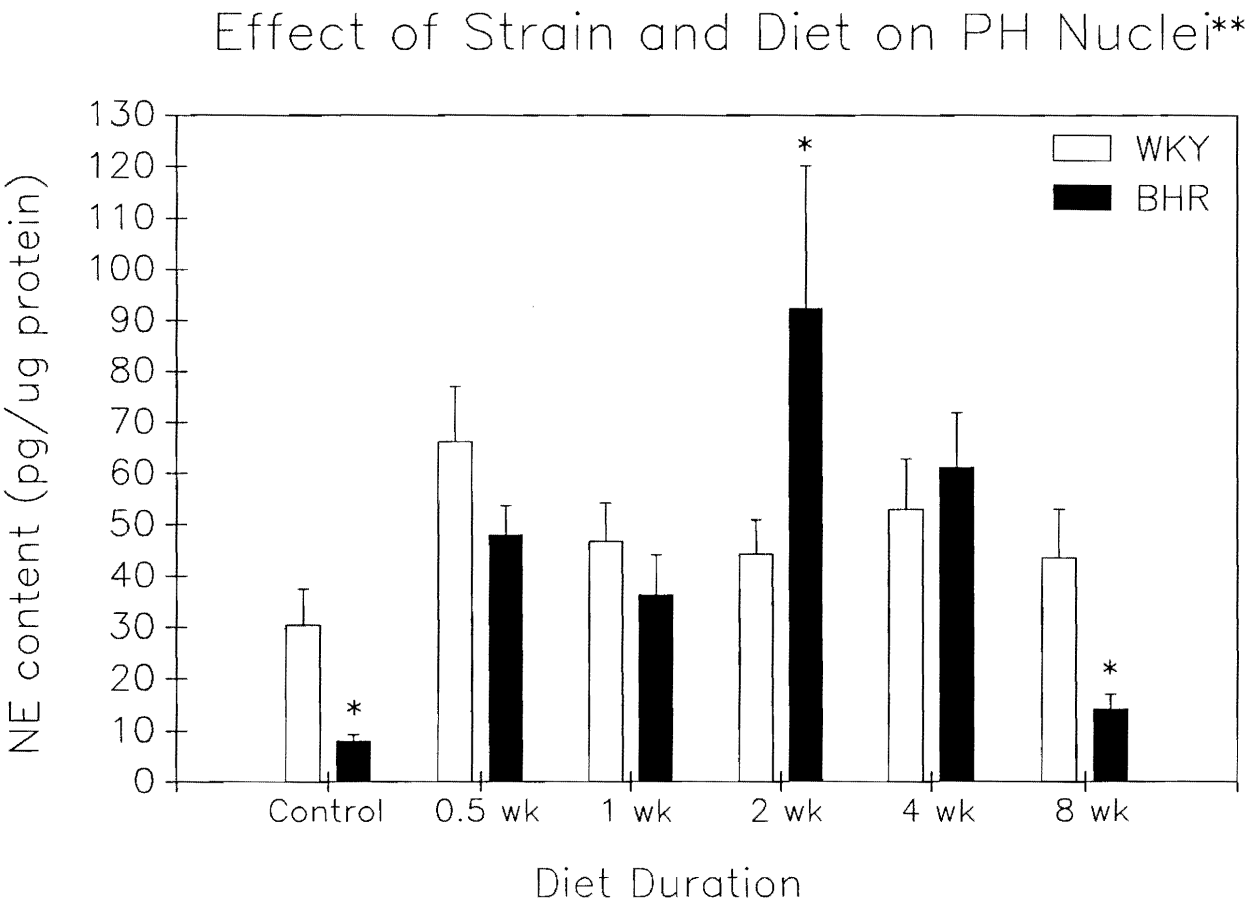

Figure 18. Mean (+/- SEM) NE concentrations of PH nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (*p<.05 for comparisons between strains and **p<.01 for strain-diet interaction)

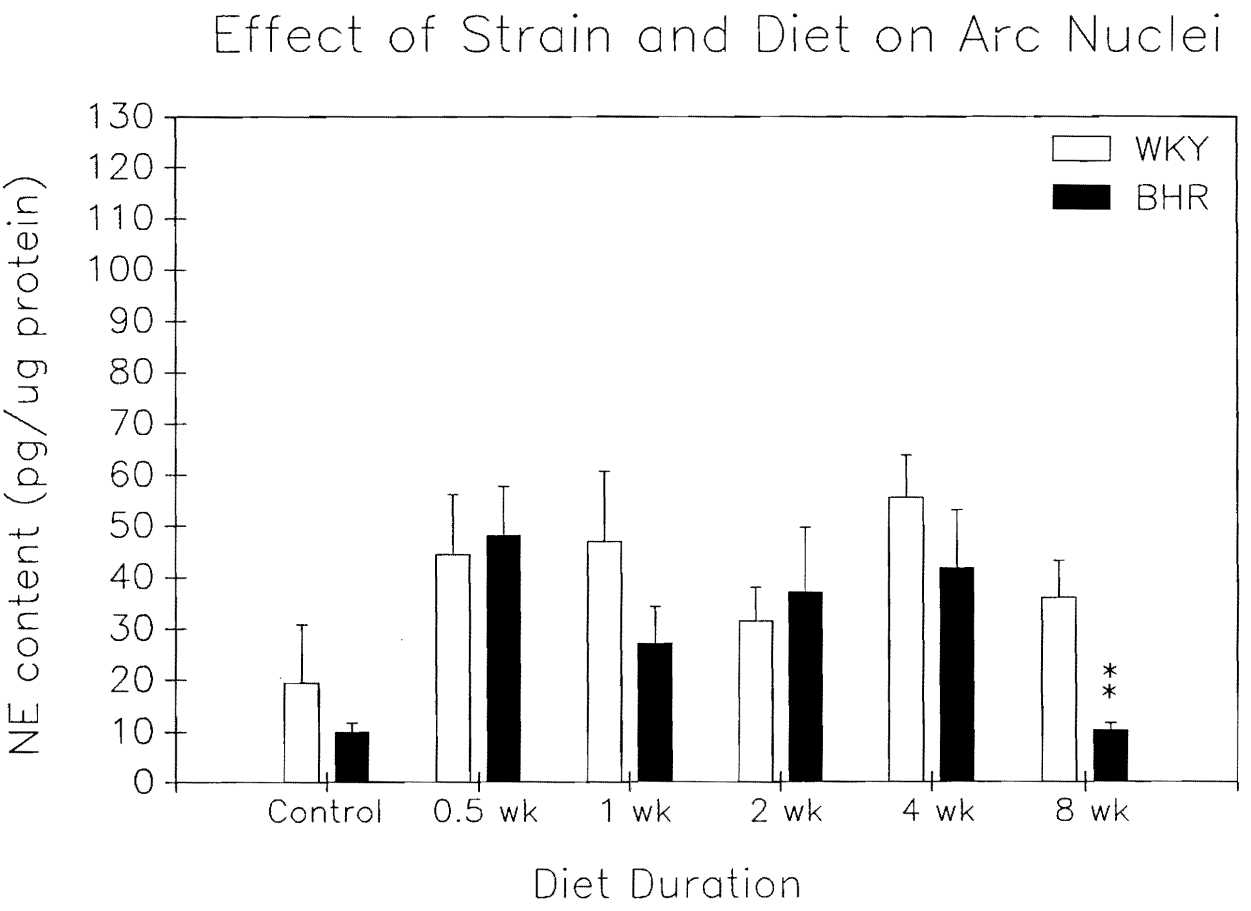

Figure 19. Mean (+/- SEM) NE concentrations of Arc nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (**p<.01 for comparisons between strains)

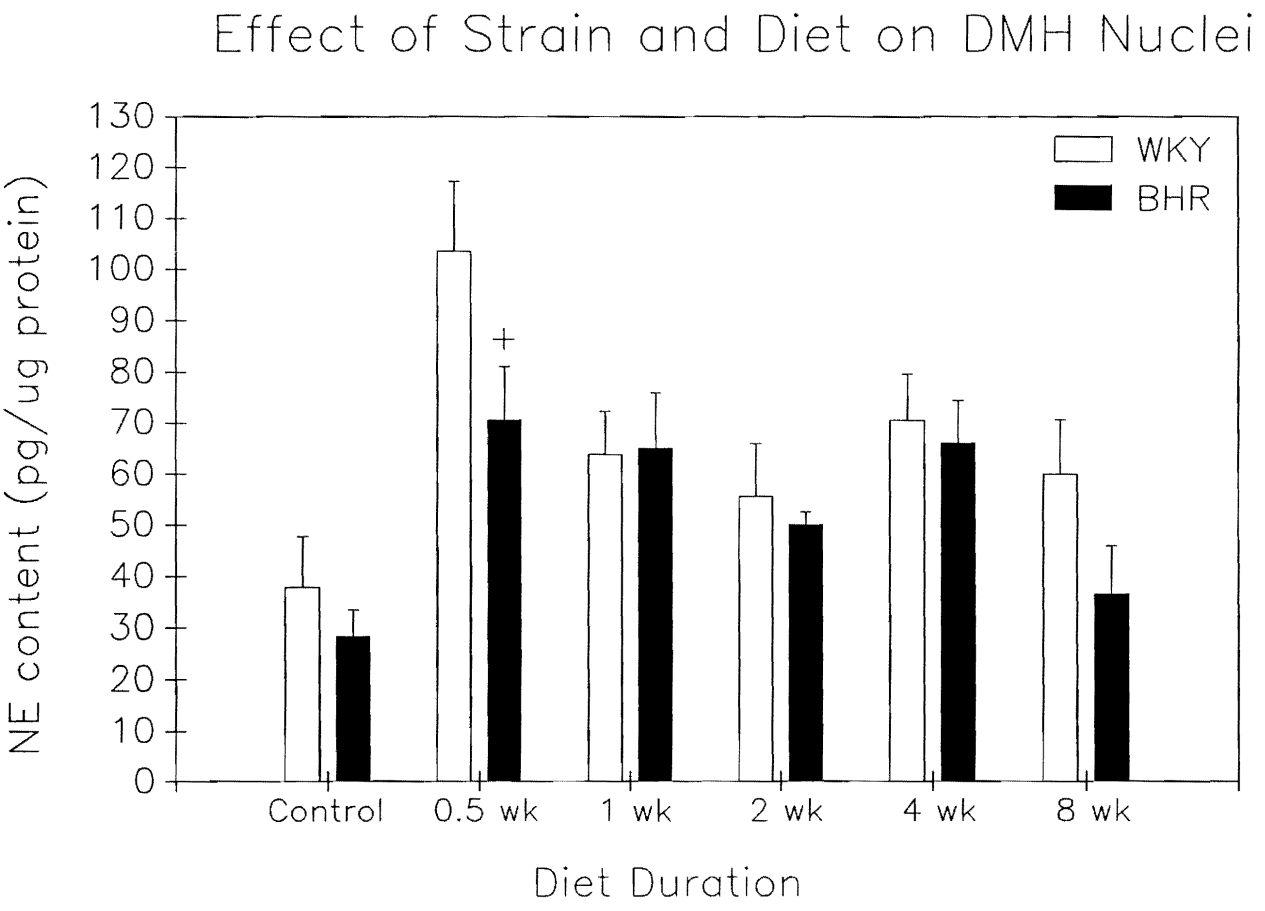

Figure 20. Mean (+/- SEM) NE concentrations of DMH nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (+p<.10 for comparisons between strains)

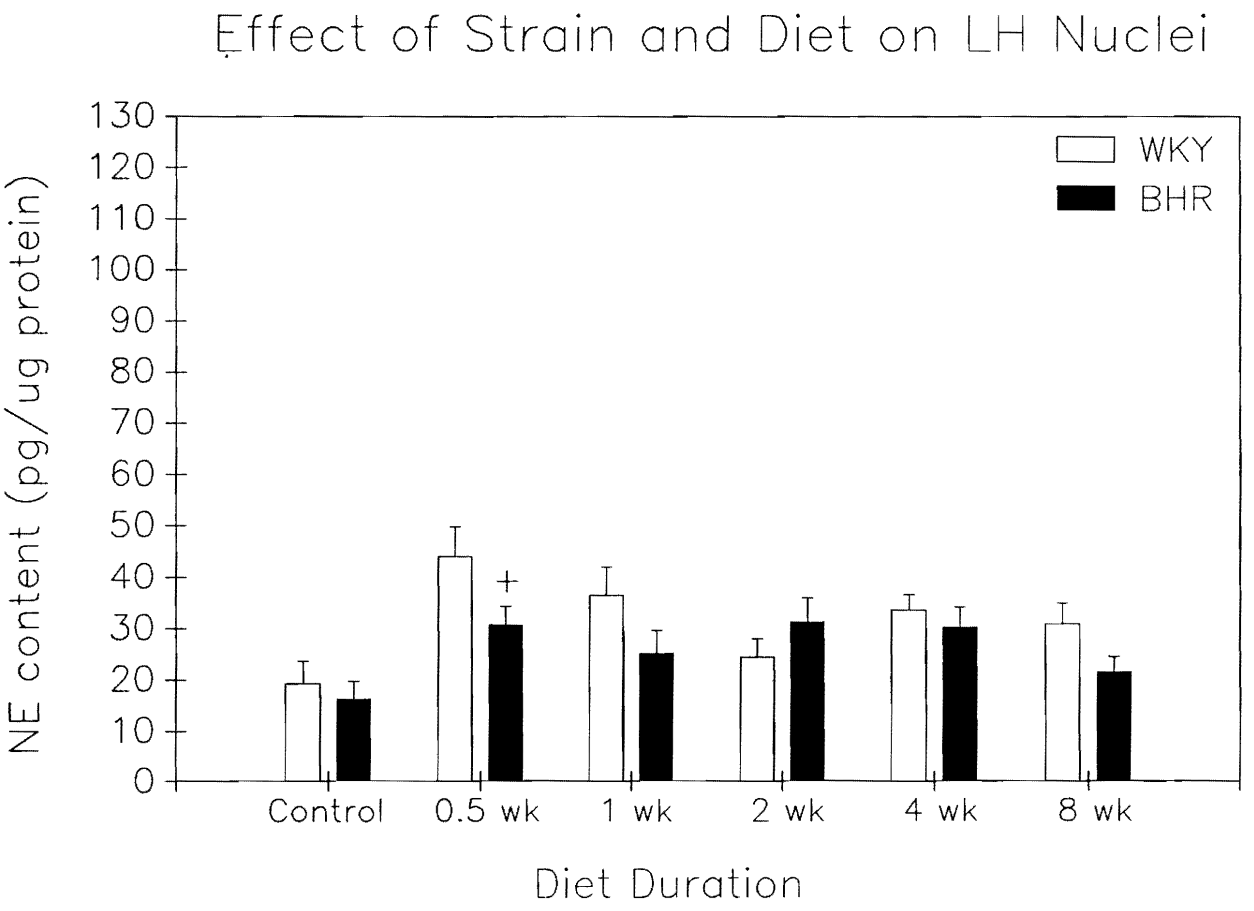

Figure 21. Mean (+/- SEM) NE concentrations of LH nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (+p<.10 for comparisons between strains)

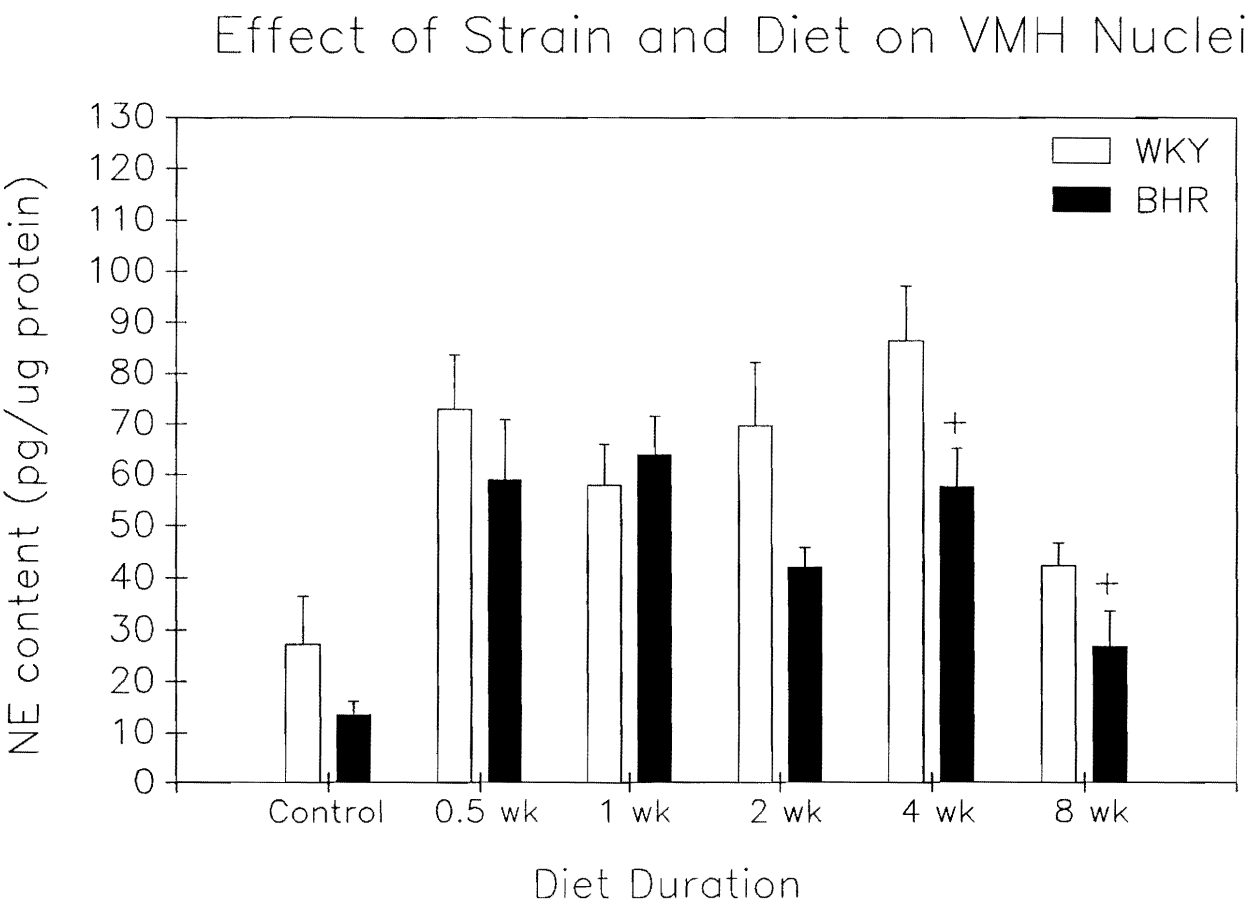

Figure 22. Mean (+/- SEM) NE concentrations of VMH nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (+$p<.10$ for comparisons between strains)

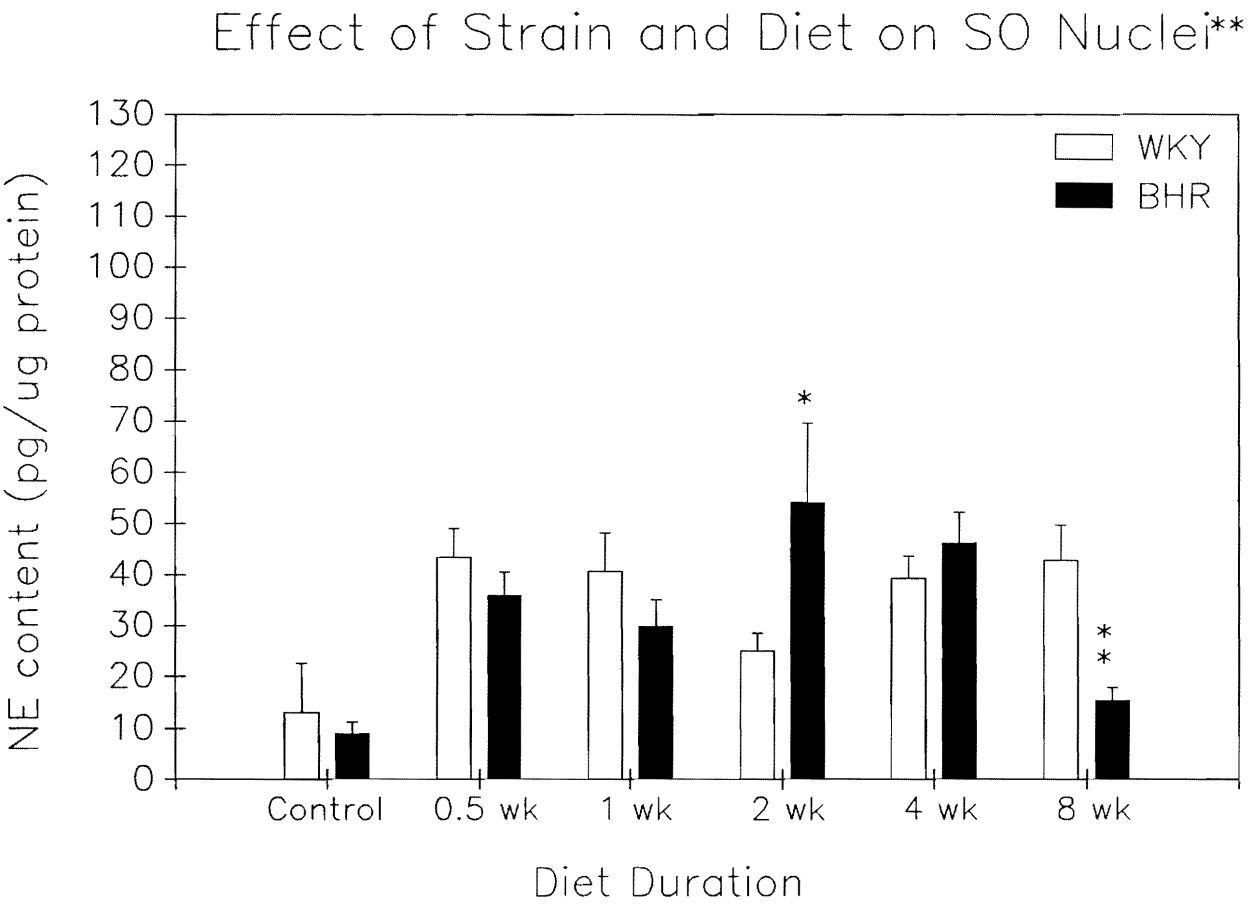

Figure 23. Mean (+/- SEM) NE concentrations of PVH nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (**p<.01 and for comparisons between strains)

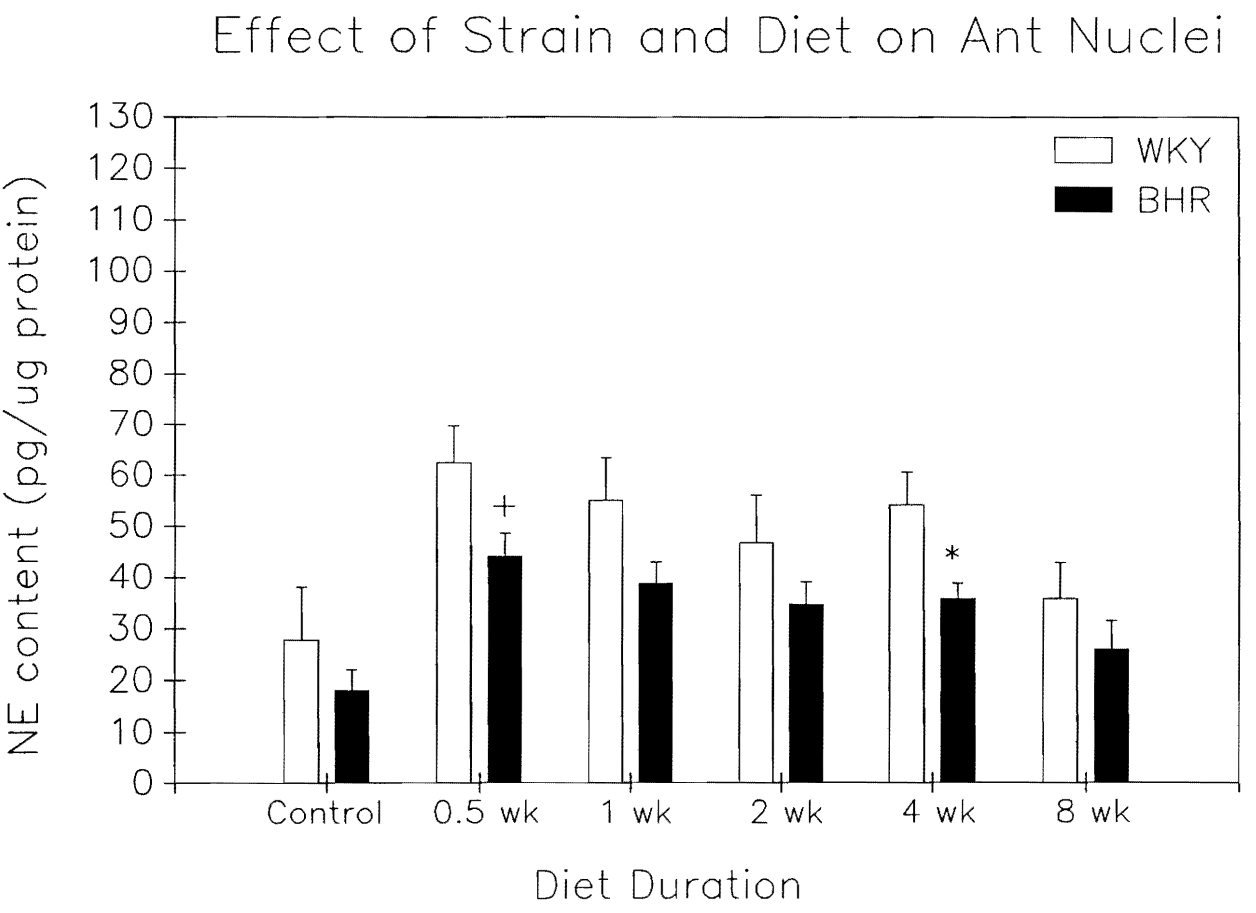

Figure 24. Mean (+/- SEM) NE concentrations of Ant nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (*p<.05 and +p<.10 for comparisons between strains)

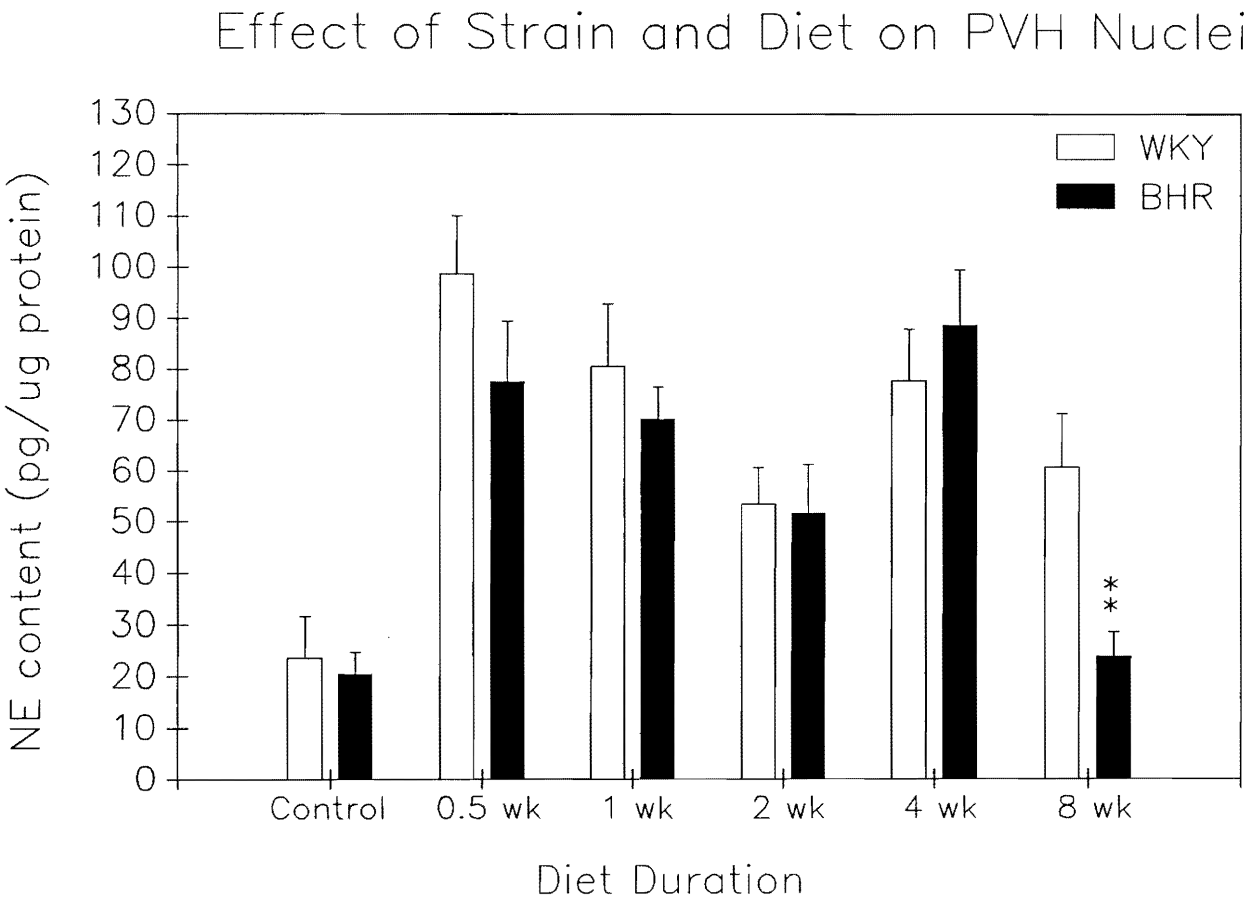

Figure 25. Mean (+/- SEM) NE concentrations of SO nuclei for WKY and BHR consuming the control diet and .5 week, 1 week, 2 week, 4 week, and 8 week high salt diets. (**p<.01 and *p<.05 for comparisons between strains and **p<.01 for strain-diet interaction)