The Relationship Between Resting Arterial Blood Pressure and Acute Postoperative Pain in Endodontic Patients

James Wayne King, DDS, MS
Endodontist in Private Practice
Chapel Hill, North Carolina
USA

Eric Bair, PhD
Research Assistant Professor
Center for Neurosensory Disorders
University of North Carolina
Chapel Hill, North Carolina
USA

Derek Duggan, DDS, MS
Assistant Professor
Department of Endodontics
University of North Carolina
Chapel Hill, North Carolina
USA

William Maixner, DDS, PhD
Distinguished Professor
Center for Neurosensory Disorders
University of North Carolina
Chapel Hill, North Carolina
USA

Asma A. Khan, BDS, PhD
Assistant Professor
Department of Endodontics and Center for Neurosensory Disorders
University of North Carolina
Chapel Hill, North Carolina
USA

Correspondence to:
Dr Asma A. Khan
1170 Old Dental Building, CB #7450
University of North Carolina
Chapel Hill, NC 27599
Email: asma_khan@dentistry.unc.edu

The results of this study were presented at the 2011 Annual Session of the American Association of Endodontists held in April 2011 in San Antonio, Texas, USA. An abstract based on this study was published in the Journal of Endodontics *(King W, Bair E, Maixner W, Khan AA. J Endod 2011;37:26)*

Aims: *To evaluate the relationship between preoperative resting arterial blood pressure and postoperative pain in patients undergoing nonsurgical root canal therapy.* ***Methods:*** *Written informed consent was obtained from normotensive patients seeking treatment for teeth with a preoperative diagnosis of pulpal necrosis and periradicular periodontitis. Preoperative resting blood pressure was recorded, and nonsurgical root canal therapy was initiated using a standardized protocol. Patients recorded their pre- and postoperative pain intensity on a 100-mm visual analog scale (VAS) for 7 days after the procedure. A linear regression model to predict postoperative VAS intensity used preoperative pain and blood pressure values as covariates. Pearson correlations were calculated to assess the relationship between the measures of preoperative blood pressure and both pre- and postoperative pain.* ***Results:*** *After controlling for preoperative pain, significant correlations were observed between preoperative systolic blood pressure and postoperative pain (*$P < .05$*), as well as between preoperative pulse pressure and postoperative pain (*$P < .005$*) on day 1.* ***Conclusion:*** *This study has provided further evidence of a functional interaction between the cardiovascular and trigeminal pain regulatory systems. Understanding this complex relationship may lead to enhanced pain management strategies.*
J OROFAC PAIN 2012;26:321–327

Key words: blood pressure, cardiovascular system, endodontics, orofacial pain

In vivo studies report an association between high resting blood pressure and a reduced sensitivity to acute pain.[1–4] This relationship between blood pressure and pain is consistent not only when hypertensive individuals (> 140/90mm Hg) are compared with normotensive individuals,[5–8] but also when higher versus lower blood pressures are compared within the normotensive range.[9–11] Correlation analysis reveals that the relationship between blood pressure and pain is linear across the normotensive blood pressure range.[10,11] Interventions that raise blood pressure, such as exercise and high-sodium diets, reduce sensitivity to experimental pain stimuli.[12,13] Furthermore, even in the absence of hypertension, the familial risk for hypertension is associated with a diminished responsiveness to acute pain, suggesting genetic contributions to the observed relationship.[14,15]

The functional interaction between blood pressure and pain has also been replicated in studies on odontogenic pain. For example, studies evaluating pulpal response to electrical stimulation show that both pain thresholds and tolerance are higher in hypertensive patients than in normotensive individuals.[5,16] In a randomized controlled clinical trial, untreated hypertensive patients were assigned to receive enalapril (an angiotensin converting enzyme-inhibitor)

or losartan (an angiotensin receptor II antagonist). Their responses to electrical pulpal stimulation was measured prior to and after drug treatment. Administration of both of these antihypertensive drugs resulted in a significant reduction in pain threshold and tolerance.[17]

Most studies evaluating hypertension-associated hypoalgesia in humans have used experimental stimuli to elicit pain.[10,11,18] Relatively fewer studies have evaluated the relationship between the cardiovascular system and clinical pain conditions.[19–22] These studies have reported that chronic pain conditions such as temporomandibular disorders (TMD) and chronic musculoskeletal complaints are less prevalent in individuals with higher resting blood pressure values as compared with those with low blood pressure values.[19–21] Individuals with high resting systolic and diastolic blood pressure are 10 times less likely to develop TMD than those with low blood pressure.[22] To date, no study has evaluated the relationship between resting arterial blood pressure and acute postoperative orofacial pain. Therefore, a prospective observational study was conducted to evaluate the relationship between resting arterial blood pressure and postoperative pain in patients undergoing nonsurgical root canal therapy. It was hypothesized that elevated preoperative resting arterial blood pressure readings are associated with diminished postoperative pain experiences.

Materials and Methods

This prospective observational study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the University of North Carolina, Chapel Hill, North Carolina, USA. Patients were recruited from the endodontic clinic in the School of Dentistry, University of North Carolina, Chapel Hill, North Carolina. Inclusion criteria were *(1)* teeth with a clinical diagnosis of pulpal necrosis as shown by a negative response to both cold (dichlorodifluoromethane Endo Ice, Hygienic) and electric sensibility testing (Sybron Endo Vitality Scanner Model 2006), and *(2)* teeth with a periradicular diagnosis of apical periodontitis as shown by the presence of a periradicular radiolucency more than twice the width of the periodontal ligament. Exclusion criteria included patients with an American Society of Anesthesiologists' physical status of 3 or greater, a periodontal pocket site around the tooth to be treated of 6 mm or deeper, the presence of an abscess or swelling around the affected tooth, persistent (> 7 days) use of medication that might alter their pain experience (such as steroids or antidepressants), and any use of analgesics up to 6 hours prior to clinical assessment.

After explaining the study and obtaining written informed consent, the investigators asked the patients to rate their spontaneous pain related to the affected tooth on a 100-mm horizontal visual analog scale (VAS) with the anchors of "no pain" and "worst pain imaginable." They reported how long they had had their tooth pain, as well as mechanical allodynia, which was described as the presence or absence of pain after gentle digital percussion. Patients were asked about the presence of facial or body pain. Facial pain was described as pain in the face, jaw, temple, in front of the ear, or in the ear, not including toothache or ear infection. Patients who reported having facial pain were asked to indicate the mean pain intensity on a 100-mm VAS. Bodily pain was described as pain in the body that lasted 1 day or more or pain in the body that has occurred several times a year due to any cause. Patients were instructed not to report aches and pains that were fleeting or attributed to known factors such as sore muscles after exercise. Those with bodily pain were asked to indicate the affected areas by drawing on a mannequin and to report the pain intensity on a 100-mm VAS.

After completion of the preoperative questionnaires, the patients' resting arterial blood pressure and heart rate were measured once using a wrist-cuff blood pressure monitor. These measurements were taken a minimum of 15 minutes after seating the patient in an upright position. The monitors used were Omron Healthcare models HEM 605 and HEM 741. Endodontic therapy was initiated using a standardized protocol. Briefly, this protocol consisted of first administering local anesthesia and then isolating the tooth with rubber dam. The root canal system was then accessed and the canals instrumented using nickel-titanium rotary and stainless steel hand instruments to the International Organization for Standardization apical size ≥ 35 with a 0.04 taper. Calcium hydroxide (Henry Schein) was placed as an intracanal medicament, and a provisional restoration (IRM, Dentsply) was placed.

Prior to dismissal, patients were given a postoperative pain diary in which they were to record their mean daily pain, as well as the most intense daily pain experienced, on a 100-mm VAS. They also recorded the presence or absence of tooth pain when they gently tapped on their tooth with a finger. The name, dose, and frequency of any analgesics taken were also recorded in the pain diary. Patients were instructed to complete the questionnaire at a consistent time daily for 1 week and were given an addressed, stamped envelope in which to mail the pain diary to the investigators after completion.

Table 1 Preoperative Blood Pressure Variables in Patients Undergoing Endodontic Therapy

	Minimum	Maximum	Mean ± SE
Systolic blood pressure (mm Hg)	94	167	126 ± 1.8
Diastolic blood pressure (mm Hg)	60	95	78 ± 1.1
Heart rate (beats/min)	47	103	72 ± 1.1
Pulse pressure (mm Hg)	20	82	48 ± 1.5
Mean arterial pressure	73	118	94 ± 1.2

SE, standard error of the mean.

Data from questionnaires and pain diaries were merged to produce an analytic data file in which each person was represented as a single unit record. A linear regression model was used to predict postoperative VAS intensity by using preoperative pain and blood pressure values as covariates. Pearson correlations were calculated to assess the relationship between the measures of preoperative blood pressure and both preoperative and postoperative pain. Then, *t* tests were used to test the null hypothesis of no association between preexisting facial pain/bodily pain and the intensity/duration of postoperative pain. A significance level of $P < .05$ was used. All data analysis was performed using *R* 2.13 (R Development core team, http://www.R-project.org). Values are reported as mean ± standard error of the mean.

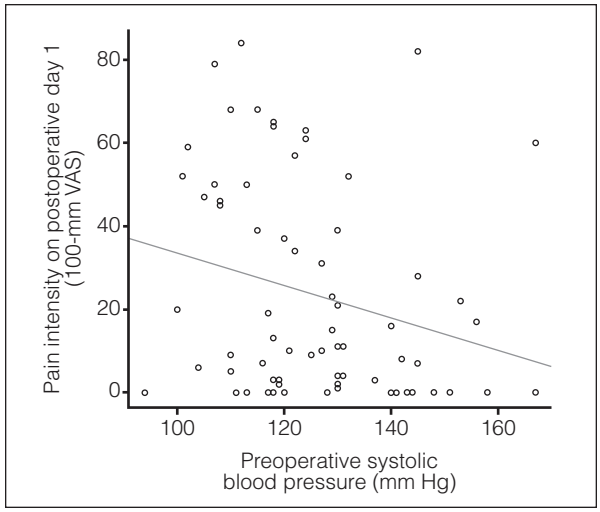

Fig 1 Scatter plot showing the negative correlation between preoperative systolic blood pressure and pain on the first postoperative day in patients undergoing endodontic therapy. The regression line is shown on the graph ($r = –0.24$, $P = .03$).

Results

A total of 93 patients was enrolled in the study. Of those, 20 patients did not return their postoperative pain diaries, and their data was therefore not included in the statistical analysis. The mean age of patients was 46 ± 1.8 years. Just over a third of the study population was male (36%). The majority of the study population described themselves as Caucasian (63%). More than twice as many maxillary teeth (51) as mandibular teeth (22) were treated during the study.

Fifty-two percent of patients had pain prior to the initiation of treatment. All of these patients reported that they had both spontaneous tooth pain and mechanical allodynia. The mean intensity of preoperative pain was reported as 27 ± 4.0 mm on the VAS. Seventy-five percent of patients had pain on postoperative day 1, with the mean pain intensity reported as 24 ± 3.1 mm on the VAS. Mechanical allodynia was reported by 47% of patients on postoperative day 1. The number of patients who reported pain, as well as the mean pain intensity, decreased steadily during the postoperative period. Forty-three percent of patients continued to have pain on postoperative day 7, with a mean pain intensity of 3 ± 0.97 mm on the VAS. Sixteen percent of patients continued to have mechanical allodynia on postoperative day 7.

Table 1 shows the preoperative blood pressure, heart rate, and pulse pressure variables. A negative correlation was noted between preoperative systolic blood pressure and pain on the first postoperative day ($r = –0.24$, $P = .03$) (Fig 1). Additionally, there was a negative correlation between preoperative pulse pressure and pain intensity on the first postoperative day ($r = –0.32$, $P = .005$) (Fig 2). No significant correlation was observed between diastolic blood pressure ($r = 0.03$, $P = .9$) or heart rate ($r = –0.06$, $P = .8$) and pain on the first postoperative day. Also, no significant correlations were observed between preoperative pain and any of the cardiovascular measures ($r < 0.1$ and $P > .5$ for all four measures).

Thirty-five percent of patients reported having facial pain, which was described as pain in the face, jaw, temple, in front of the ear, or in the ear (not including toothache or ear infection). The mean

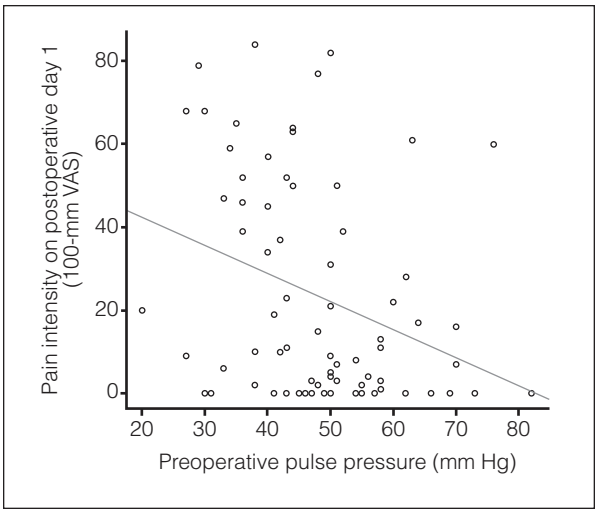

Fig 2 Scatter plot showing the negative correlation between preoperative pulse pressure and pain on the first postoperative day in patients undergoing endodontic therapy. The regression line is shown on the graph ($r = -0.32$, $P = .005$).

intensity of the facial pain reported was 48 ± 6.6 mm on the VAS. Twenty-five percent of patients reported having persistent or chronic body pain, and the mean intensity of body pain was 48 ± 4.4 mm on the VAS. The presence of facial and/or body pain was not associated with the intensity or duration of postoperative pain after endodontic therapy ($P > .05$ for all t tests performed).

Discussion

Endogenous pain-regulatory systems composed of both inhibitory and facilitatory pathways modulate a person's ability to adapt to acute and persistent pain. The immediate response to a noxious stimulus engages the inhibitory pathways, allowing the person to escape from the source of injury (or noxious stimulus) without experiencing intense pain.[23,24] Once the acute danger has passed, the facilitatory pathways amplify the pain, which helps avoid additional injury, encourages rest, and facilitates healing. Under normal conditions, when pain persists beyond the initial healing period, inhibitory pathways are once again engaged, which enables the resumption of the normal activities necessary for survival.[23]

An important component of the endogenous pain-regulatory system is the functional interaction between the cardiovascular and pain-regulatory systems, which results in an association between elevated resting blood pressure and diminished acute pain sensitivity. There is substantial overlap between the brain regions underlying the control of the cardiovascular system and those that contribute to antinociception. The mechanisms that underlie the interaction between blood pressure and pain sensitivity include baroreceptor-, endogenous opioid-, and noradrenergic-related mechanisms. It has been proposed that *(a)* pain increases sympathetic arousal, which results in increased blood pressure, *(b)* this increased blood pressure also results in increased baroreceptor stimulation, which in turn *(c)* activates the inhibitory pathways and results in reduced pain sensitivity, thus facilitating the return to a normal homeostatic state.[25,26] Several lines of evidence support the role of baroreceptors in the blood pressure/pain sensitivity relationship. Electrical or pharmacologic stimulation of baroreceptors afferents induces antinociception.[27–29] Surgical denervation of these afferents eliminates the hypoalgesia displayed in hypertensive animals and produces hyperalgesia in normotensive animals.[27,30] It is important to note that baroreceptor stimulation modulates both the sensory and affective components of pain.

Endogenous opioids, important components of the pain-regulatory system, are proposed to mediate the interaction between the cardiovascular and pain-regulatory systems. Elevated blood pressure is associated with increased plasma levels of β endorphin in experimental animals and humans.[31] Naloxone, an opioid antagonist, reverses the hypoalgesia seen in hypertensive animals.[1,32] Some clinical studies have reported that opioid blockade reverses the relationship between blood pressure and pain sensitivity.[11,33–35] This suggests that in humans, the interaction between blood pressure and pain sensitivity is mediated at least in part by opioid mechanisms.

Central noradrenergic pathways are important players in the descending pain-inhibitory pathways and regulation of the cardiovascular system. Structures in the central nervous system, such as the nucleus tractus solitarius, nucleus raphe magnus, periaqueductal gray, rostral ventrolateral medulla, and locus coeruleus, are involved in the cardiovascular and pain-regulatory relationship. All of these structures are potential sources of noradrenergic influences on descending pain modulation.[24,26,36] Animal studies have provided substantial evidence of the role of supraspinal alpha-2-adrenergic descending pathways in mediating the relationship between blood pressure and pain sensitivity. For example, a pharmacologic blockade of the adrenergic receptors or lesioning of the brainstem adrenergic system reverses or eliminates hypertension-associated antinociception.[36–38] In humans, higher blood pressure is associated with both elevated pain tolerance and

increased blood levels of norepinephrine.[37,38] However, there is no direct evidence of involvement of the α-2-adrenergic system in the blood pressure/pain sensitivity interaction in humans.[6]

To the authors' knowledge, this is the first prospective study demonstrating a functional interaction between the cardiovascular system and postoperative pain sensitivity following endodontic therapy. The frequency of postoperative pain observed in this study was similar to that reported in other studies of endodontic patients.[39–43] The factors known to be correlated with postoperative pain include preoperative swelling, tenderness to percussion prior to initiation of treatment, previous chronic pain problems, and the presence of preoperative pain in the tooth.[44–46] The authors did not recruit patients who presented with abscesses or swelling around the affected tooth. While other studies suggest that previous chronic pain conditions are associated with increased postoperative pain, this study found no significant correlation between the presence of facial or bodily pain and the intensity or duration of postoperative pain. This may be due to the fact that the study was underpowered, since only 25% of the subjects in the present study reported chronic or persistent pain. Prior studies have reported that the administration of antihypertensive medications result in decreased pain sensitivity.[47] None of the subjects in this study were taking antihypertensive medications.

While most studies evaluating the interaction between the cardiovascular and pain-regulatory systems have reported an association between elevated blood pressure and reduced pain sensitivity, fewer studies have reported the opposite.[48–50] For example fibromyalgia patients have higher resting systolic and diastolic blood pressure compared with pain-free controls.[48] Hypertension is reported to be a risk factor for migraine chronification.[49,50] It has been proposed that hypertension exacerbates the effects of migraine on the vascular wall and thus enhances the endothelial dysfunction in cerebral vasculature.[49] Results of a recent systematic review suggest that angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may have a role in migraine prophylaxis.[50]

This study has several limitations. Preoperative arterial blood pressure was measured only once in this study and was done so using a wrist-cuff monitor. A mean of at least three readings obtained using an arm cuff monitor would have been a better estimate of resting blood pressure. Comparison of blood pressure values and pain ratings prior to treatment would then have provided valuable information. The study also did not obtain information about parental history of hypertension and exercise history. Both of these are known to affect the relationship between blood pressure and pain sensitivity.[13–15] While patients recorded their postoperative pain intensity, they were not asked to record the period of time for which they experienced pain. In the present study, mechanical allodynia was defined as pain after gently tapping the tooth with a finger. Quantitative measurement of mechanical allodynia in the pre- and postoperative periods would have been a better approach. The study also did not evaluate the subjects for anxiety or stress, which may have affected elevated blood pressure and pain sensitivity.[51,52] In future studies, a consultation appointment would provide an opportunity for measuring blood pressure in a more relaxed environment. While the results of this study support an interaction between the cardiovascular system and acute postoperative pain, future studies are needed to elucidate the mechanism underlying this interaction. Continuing this line of research will enhance our ability to manage and/or prevent odontogenic pain associated with clinical procedures.

Acknowledgments

This work was supported by the School of Dentistry, University of North Carolina, Chapel Hill North Carolina. The authors thank Drs Lauren Kennedy and Stephen Richardson for their help in recruiting subjects.

References

1. Zamir N, Segal M. Hypertension-induced analgesia: Changes in pain sensitivity in experimentally hypertensive rats. Brain Res 1979;160:170–173.
2. Zamir N, Simantov T, Segal M. Pain sensitivity and opioid activity in genetically and experimentally hypertensive rats. Brain Res 1980;184:299–310.
3. Maixner W, Touw K, Brody M, Gebhart G, Long J. Factors influencing the altered pain perception in the spontaneously hypertensive rat. Brain Res 1982;237:137–145.
4. Maixner W, Randich A. Role of the right vagal nerve trunk in antinociception. Brain Res 1984;188:374–377.
5. Zamir N, Shuber E. Altered pain perception in hypertensive humans. Brain Res 1980;201:471–474.
6. Rosa C, Ghione S, Panattoni E, Mezzasalma L. Comparison of pain perception in normotensives and borderline hypertensives by means of a tooth pulp stimulation test. J Cardiovasc Pharmacol 1986;8:s125–s127.
7. Ghione S, Rosa C, Mezzasalma L, Panattoni E. Aterial hypertension is associated with hypalgesia in humans. Hypertension 1988;12:491–497.
8. Sheps D, Bragdon E, Gray T, Ballenger M, Usedom J, Maixner W. Relationship between systemic hypertension and pain perception. Am J Cardiol 1992;70:3F–5F.

9. Elbert T, Rockstroh B, Lutzenberger W, Kessler M, Pietrowsky R, Birbaumer N. Baroreceptor stimulation alters pain sensation depending on tonic blood pressure. Psychophysiology 1988;25:25–29.
10. Bruehl S, Carlson C, McCubbin J. The relationship between pain sensitivity and blood pressure in normotensives. Pain 1992;48:463–467.
11. McCubbin JA, Bruehl S. Do endogenous opioids mediate the relationship between blood pressure and pain sensitivity in normotensives? Pain 1994;57:63–67.
12. Ditto BE, Edwards MC, Miller S, D'Antono B, Blum S. The effects of sodium loading on blood pressure and pain responses to the cold pressor test. J Psychosom Res 1993; 3:771–780.
13. Kemppainen P, Pertovaara A, Huopaniemi T, Johansson G, Karonen SL. Modification of dental pain and cutaneous thermal sensitivity by physical exercise in man. Brain Res 1985;360:33-40.
14. al'Absi M, Buchanan TW, Lovallo WR. Pain perception and cardiovascular responses in men with positive parental history for hypertension. Psychophysiology 1996;33:655–661.
15. France CR, Froese SA, Stewart JC. Altered central nervous system processing of noxious stimuli contributes to decreased nociceptive responding in individuals at risk for hypertension. Pain 2002;98:101–108.
16. Guasti L, Cattaneo R, Rinaldi O, et al. Twenty-four-hour noninvasive blood pressure monitoring and pain perception. Hypertension 1995;25:1301–1305
17. Guasti L, Zanotta D, Diolisi A, et al. Changes in pain perception during treatment with angiotensin converting enzyme-inhibitors and angiotensin II type 1 receptor blockade. J Hypertens 2002;20:485–491.
18. Maixner W, Fillingim R, Kincaid S, Sigurdsson A, Harris B. Relationship between pain sensitivity and resting arterial blood pressure in patients with painful temporomandibular disorders. Psychosom Med 1997:59;503–511.
19. Hagen K, Stovner LJ, Vatten L, Holmen J, Zwart JA, Bovim G. Blood pressure and risk of headache: A prospective study of 22,685 adults in Norway. J Neurol Neurosurg Psychiatry 2002;72:463–466.
20. Hagen K, Zwart J-A, Holeman J, Svebak S, Bovim G, Stovner LJ. Does hypertension protect against chronic musculoskeletal complaints? The Nord-Trondelag Health Study. Arch Intern Med 2005;165:916–922.
21. Stovner LJ, Hagen K. Hypertension-associated hypalgesia: A clue to the comorbidity of headache and other pain disorders. Acta Neurol Scand 2009;120:46–50.
22. Diatchenko L, Anderson AD, Slade GD, et al. Three major haplotypes of the ADRB2 adrenergic receptor define psychological profile, blood pressure, and the risk for development of a common musculoskeletal pain disorder. Am J Med Genet B Neuropsychiatr Genet 2006;141:449–462.
23. Maixner W. Pain modulatory systems. In: Sessle BJ, Lavigne GJ, Lund JP, Dubner R (eds). Orofacial Pain. Chicago: Quintessence, 2008:61–68.
24. Millan MJ. Descending control of pain. Prog Neurobiol 2002;66:355–474.
25. Zamir N, Maixner W. The relationship between cardiovascular and pain regulatory systems. Ann NY Acad Sci 1986;467:371–384.
26. Ghione S. Hypertension-associated hypalgesia: Evidence in experimental animals and humans, pathophysiological mechanisms, and potential clinical consequences. Hypertension 1996;28:494–504.
27. Dworkin B, Filewich R, Miller N, Craigmyle N, Pickering T. Baroreceptor activation reduces reactivity to noxious stimulation: Implications in hypertension. Science 1979; 205:1299–1301.
28. Takeda M, Tanimoto T, Ojima K, Matsumoto S. Suppressive effects of vagal afferents on the activity of the trigeminal spinal neurons related to the jaw-opening reflex in rats: Involvement of the endogenous opioid system. Brain Res Bull 1998;47:49–56.
29. Bossut DF, Maixner W. Effects of cardiac vagal afferent electrostimulation on the responses of trigeminal and trigeminothalamic neurons to noxious orofacial stimulation. Pain 1996;65:101–109.
30. Maixner W, Touw K, Brody M, Gebhart G, Long J. Factors influencing the altered pain perception in the spontaneously hypertensive rat. Brain Res 1982;237:137–145.
31. Rosa C, Ghione S, Mezzasalma L, et al. Relationship between pain sensitivity, cardiovascular reactivity to cold pressor test, and indexes of activity of the adrenergic and opioid system. Clin Exp Theory 1988;10:383–390.
32. Maixner W, Touw K, Brody M, Gebhart G, Long J. Factors influencing the altered pain perception in the spontaneously hypertensive rat. Brain Res 1982;237:137–145.
33. Schobel HP, Handwerker HO, Schmieder RE, Huesser K, Dominiak P, Luft FC. Effects of naloxone on hemodynamic and sympathetic nerve responses to pain in normotensives vs borderline hypertensive men. J Auton Nerv Syst 1998;69:49–55.
34. Frew AK, Drummond PD. Negative affect, pain and sex: The role of endogenous opioids. Pain 2007;132(suppl 1):S77–S85.
35. Lewkowski MD, Young SN, Ghosh S, Ditto B. Effects of opioid blockade on the modulation of pain and mood by sweet taste and blood pressure in young adults. Pain 2008;135:75–81.
36. Randich A, Maixner W. Interactions between cardiovascular and pain regulatory systems. Neurosci and Behav Rev 1984;8:343–367.
37. Bruehl S, Burns JW, Chung OY, et al. Hypoalgesia associated with elevated resting blood pressure: Evidence for endogenous opioid involvement. J Behav Med 2010;33:168–176.
38. Chobanian AV, Gavras H, Melby JC, Gavras I, Jick H. Relationship of basal plasma norepinephrine to blood pressure, plasma renin activity, mineralocorticoids, and plasma volume in essential hypertension. Trans Assoc Am Physicians 1978;91:368–380
39. Seltzer S, Bender IB, Ehrenreich J. Incidence and duration of pain following endodontic therapy. Relationship to treatment with sulfonamides and to other factors. Oral Surg Oral Med Oral Pathol 1961;14:74–82.
40. Fox J, Atkinson J, Dinin A, et al. Incidence of pain following one-visit endodontic treatment. Oral Surg Oral Med Oral Pathol 1970;30:123–130.
41. Mulhern JM, Patterson SS, Newton CW, Ringel AM. Incidence of postoperative pain after one-appointment endodontic treatment of asymptomatic pulpal necross in single-rooted teeth. J Endod 1982;8:370–375.
42. Georgopoulou M, Anastassiadis P, Sykaras S. Pain after chemomechanical preparation. Int Endod J 1986;19: 309–314.
43. Sathorn C, Parashos P, Messer H. The prevalence of postoperative pain and flare-up in single and multiple-visit endodontic treatment: A systematic review. Int Endod J 2008;41:91–99.

44. Polycarpou N, Ng YL, Canavan D, Moles DR, Gulabivala K. Prevalence of persistent pain after endodontic treatment and factors affecting its occurrence in cases with complete radiographic healing. Int Endod J 2005;38:169–178.
45. Glennon JP, Ng YL, Setchell DJ, Gulabivala K. Prevalence of and factors affecting postpreparation pain in patients undergoing two-visit root canal treatment. Int Endod J 2004;37:29–37.
46. El Mubarak AH, Abu-bakr NH, Ibrahim YE. Postoperative pain in multiple-visit and single-visit root canal treatment. J Endod 2010;36:36–39.
47. Guasti L, Cattaneo R, Rinaldi O, et al. Twenty-four-hour noninvasive blood pressure monitoring and pain perception. Hypertension 1995;25:1301–1305.
48. Kulshreshtha P, Gupta R, Yadav RK, Bijlani RL, Deepak KK. A comprehensive study of autonomic dysfunction in the fibromyalgia patients. Clin Auton Res 2011;22:117–122.
49. Barbanti P, Aurilia C, Egeo G, Fofi L. Hypertension as a risk factor for migraine chronification. Neurol Sci 2010;31(suppl 1):S41–S43.
50. Gales BJ, Bailey EK, Reed AN, Gales MA. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for the prevention of migraines. Ann Pharmacother 2010;44:360–366.
51. Jeter CR, Bush JP, Porter JH. Situational anxiety and blood pressure lability in the physician's office. Clin Exp Hypertens A 1988;10:169–185.
52. Clark WC, Yang JC, Janal MN Altered pain and visual sensitivity in humans: The effects of acute and chronic stress. Ann NY Acad Sci 1986;467:116–129.