A Calibrated Method of Massage Therapy Decreases Systolic Blood Pressure Concomitant With Changes in Heart Rate Variability in Male Rats

Kurt A. Spurgin, DC, PhD,[a] Anthony Kaprelian, BS,[a] Roberto Gutierrez, BS,[a] Vidyasagar Jha, BS,[a] Christopher G. Wilson, PhD,[b] Abigail Dobyns, BS,[b] Karen H. Xu, BS,[c] and Margarita C. Curras-Collazo, PhD[a]

Abstract

Objective: The purpose of this study was to develop a method for applying calibrated manual massage pressures by using commonly available, inexpensive sphygmomanometer parts and validate the use of this approach as a quantitative method of applying massage therapy to rodents.

Methods: Massage pressures were monitored by using a modified neonatal blood pressure (BP) cuff attached to an aneroid gauge. Lightly anesthetized rats were stroked on the ventral abdomen for 5 minutes at pressures of 20 mm Hg and 40 mm Hg. Blood pressure was monitored noninvasively for 20 minutes following massage therapy at 5-minute intervals. Interexaminer reliability was assessed by applying 20 mm Hg and 40 mm Hg pressures to a digital scale in the presence or absence of the pressure gauge.

Results: With the use of this method, we observed good interexaminer reliability, with intraclass coefficients of 0.989 versus 0.624 in blinded controls. In Long-Evans rats, systolic BP dropped by an average of 9.86% ± 0.27% following application of 40 mm Hg massage pressure. Similar effects were seen following 20 mm Hg pressure (6.52% ± 1.7%), although latency to effect was greater than at 40 mm Hg. Sprague-Dawley rats behaved similarly to Long-Evans rats. Low-frequency/high-frequency ratio, a widely-used index of autonomic tone in cardiovascular regulation, showed a significant increase within 5 minutes after 40 mm Hg massage pressure was applied.

Conclusions: The calibrated massage method was shown to be a reproducible method for applying massage pressures in rodents and lowering BP. (J Manipulative Physiol Ther 2017;40:77-88)

Key Indexing Terms: *Musculoskeletal Manipulations; Sprague-Dawley Rat; Long-Evans Rat; Diastolic Blood Pressure; Stress; Sympathetic Nervous System; Parasympathetic Tone*

Introduction

Approximately 30% of adults in the United States have high blood pressure (BP),[1] resulting in an annual cost of more than $76.6 billion in health care services and missed work.[2] The etiology of essential hypertension is still unclear, although both the renin-angiotensin system[3-5] and the sympathetic nervous system (SNS)[6-8] appear to play important roles the development of high BP.

Although pharmacologic approaches to the management of hypertension via the renin-angiotensin system and the SNS have proven to be effective, side effects, such as angioedema, headache, hypotension, and dizziness, are common.[9,10] There are relatively few well-studied, nonpharmacologic options for the prevention and treatment of hypertension.[11-13] One potential nonpharmacologic treatment option, massage, has been associated with a significant impact on BP and autonomic nervous system activity. In humans, moderate pressure massage can decrease heart rate and BP while increasing vagal afferent activity as measured by heart rate variability.[14,15] Lumbar spine manipulation has been shown to increase lumbar parasympathetic nervous system output in patients with pain.[16] Moderate pressure massage in humans has also been shown to decrease self-reported stress while increasing delta activity and decreasing alpha and beta activity

[a] Department of Cell Biology & Neuroscience, University of California, Riverside, CA.
[b] Division of Physiology, Loma Linda University, Loma Linda, CA.
[c] Statistical Consulting Collaboratory, University of California, Riverside, CA.
Corresponding author: Kurt Spurgin, DC, PhD, Department of Cell Biology & Neuroscience, University of California, Riverside, 900 University Ave, Riverside, CA 92521. Tel.: +1 760 578 5651. (e-mail: *kurtspurgindc@gmail.com*).

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on electroencephalography, suggesting a relaxation response after only 10 minutes of moderate pressure massage.[17] Massage-like stroking of the skin in rats has been reported to increase withdrawal latency to noxious stimuli,[18] which is a sedative response,[19] indicating benefit for pain modulation. Similar manipulation was shown to produce an inhibitory effect on the cardiovascular excitatory response[20] and a reduction in both BP and heart rate.[21,22] Studies on the effects of manual therapies have emphasized that the responses vary significantly, depending on the type, location, and strength of the manual stimulation procedures.[20-23] Importantly, negative side effects from manual therapy are exceedingly rare.[24]

Relatively few studies have utilized animal models to examine the specific mechanisms underlying how massage therapies impact BP. One possible mechanism is revealed from studies using related stimulation (cutaneous brushing of the chest in rats), which significantly decreases adrenal efferent nerve activity and catecholamine secretion.[20,23] The lack of mechanistic studies performed in animals may be attributed to the lack of an inexpensive, precise, and repeatable technique for applying calibrated massage pressures in small rodents. Several studies reported in the early 1990s had performed massage-like stroking of the skin in rats. Unfortunately, the massage pressures used were not calibrated[18] or were estimated and compared with pressures subsequently applied to a balloon connected to a pressure gauge.[21,22] These past studies produced interesting results and demonstrated significant differences between the applications of mild and moderate estimated pressures. However, we recognized the need to develop a technique for applying calibrated massage pressures to rodents with improved interexaminer reliability for our own studies.

The purpose of this study was to develop a method for applying calibrated manual massage pressures using commonly available, inexpensive sphygmomanometer parts and validate the use of this approach as a quantitative method of applying massage therapy to rodents. In this study, we tested the hypothesis that this simple method would provide for good interexaminer reliability, as determined via the Generalizability Theory method. We further hypothesized that this calibrated method of applying massage pressures in rats would decrease BP and increase heart rate variability, which is an index of autonomic tone in cardiovascular regulation. It is our hope that this technique can be employed easily and reliably to quantify the amount of pressure applied during manual massage in small animals and should enable a wider range of animal laboratories to examine mechanisms underlying the effects of massage therapy in rodents.

Methods

Animals

All animals were maintained in accordance with the guidelines in National Institutes of Health Guide for the Care and Use of Laboratory Animals. Thirteen male Sprague-Dawley and 8 Long-Evans rats (300-500 g) were group-housed 2 to 3 per cage in standard polycarbonate plastic cages with heat-treated pine shavings as bedding. Food pellets (Purina Lab Diet; Nestlé Purina Petcare, St. Louis, MO) and water were provided *ad libitum* except during the experimental period. Temperature was maintained at 21 ± 2°C and relative humidity at 50% ± 10% under a 12/12-hour light/dark cycle (lights on from 7:00 to 19:00 hours). All experiments were designed in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the Institutional Animal Care and Use Committee, University of California (Riverside, CA).

Massage Therapy

Massage therapy was performed under light anesthesia (1.75% isoflurane, 1 L/min oxygen [O_2]) after a brief induction (5% isoflurane: 95% O_2; rate of air flow = 2 L/min). Each rat was laid on its back inside a ventilated fume hood and under a heat lamp, which was placed 20 inches above the rat. A neonatal BP cuff (Trimline Tempa-Kuff, Welch Allyn, size 1) was modified via a midline cut that retained only the inflatable bladder (Fig 1A). The cuff was attached to a standard clinical aneroid gauge (Tycos, Skaneateles Falls, NY) via a Luer connector (Fig 1B). These components were chosen because of their durability, ease of cleaning, and ready availability. The bladder was inflated to 100 mm Hg and held lightly by the edges. The hook-and-loop side of the neonatal cuff was positioned at the distal index finger to provide appropriate friction in anesthetized rats, and the smooth side of the cuff was used to make contact with the rats' fur (Fig 2A). An investigator could wrap his or her index finger with a "loop surface" that would attach to the hook surface on the neonatal cuff to secure the cuff to the index finger, although this was not necessary in this study.

When applying the study method in the rats, the animals were stroked on the ventral abdomen rostrally to caudally from just below the sternum to the pelvis. The bladder was then removed from the animal and positioned just below the sternum for the next stroke. Care was taken to ensure that when using the technique only the bladder surface contacted the animal and that neither the experimenter's hand nor the sphygmomanometer tubing came in contact with the animal during the procedure. A digital timer was used to monitor stroke rate, and massage was applied at a rate of 60 strokes per minute (1 stroke per second) for 5 minutes (Fig 2B). The neonatal cuff was cleaned with 75% ethanol between therapy sessions.

Massage pressures were monitored as net pressure above 100 mm Hg baseline setting, and therapy was delivered at pressures of 40 mm Hg and 20 mm Hg. A no therapy session was performed 5 to 7 days prior to manipulation of the treated rats to remove any effect of anesthesia and the experimental environment. Therefore, each rat received 3