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Applications of Telemetry in Small Laboratory Animals for Studying Cardiovascular Diseases

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1. Introduction

Telemetry is a state-of-the-art method of monitoring physiological functions in awake and freely moving laboratory animals, while minimizing stress artefacts. Currently, telemetry systems are employed for measurements of blood pressure, heart rate, blood flow, electrocardiogram, respiratory rate, sympathetic nerve activity, body temperature and many other biological signals in a wide range of animal species including rats, mice, dogs, rabbits, gerbils, hamsters, monkeys, guinea pigs and pigs (Kramer et al., 2001; Butz & Davisson, 2001; Galvin et al., 2006; Moons et al., 2007; Hess et al., 2007; Shaw et al., 2007; Greene et al., 2008). Although telemetry technology has existed for at least 50 years, it has only been in the last decade or so that affordable, reliable, and user friendly commercial products have been available for monitoring physiological signals in the laboratory setting. In particular, the use of telemetry for measuring blood pressure in mice and rats has aided researchers in discovering fundamental mechanisms involved in the physiology and pathophysiology of cardiovascular diseases such as hypertension, heart failure and pre-eclampsia (Kramer & Kinter, 2003; Zimmerman et al., 2004; Hoffman et al., 2008, Burmeister et al., 2011). Moreover, drug discovery for treating hypertension has significantly benefited from telemetry since it allows for drug effects to be investigated chronically and longitudinally. In the first part of this chapter, we will discuss the significant contributions of telemetry towards advancing the field of cardiovascular physiology/pathophysiology, emphasizing chronic studies using several experimental models of hypertension. In the second part, we will discuss the benefits of using telemetry in regards to animal welfare and some strategies to refine the telemetry technique in order to reduce the cost and the number of animals used in experiments while improving animal welfare.

2. Use of telemetry in rodents for cardiovascular research

The techniques for measuring arterial blood pressure in experimental animals have improved considerably over the past decades, and several methods are now available. Arterial blood pressure is often measured to assess the reactivity of the cardiovascular system to a treatment (e.g., to a drug or stress) or as an endpoint in itself (e.g., studies of hypertension). The manner in which blood pressure is measured varies from laboratory to laboratory, and the specific values obtained, their reliability and appropriate interpretation, are strongly influenced by the approach selected. These approaches can be divided into indirect and direct methods.

Indirect methods refer to non-invasive methods of blood pressure measurement. Until recently, the most common indirect method for measuring arterial blood pressure in rodents has been the tail-cuff plethysmography, which consists of a tail-cuff device in combination with blood flow sensor (Kim et al., 1995). The major drawbacks of the tail-cuff method are that it measures only systolic pressure and requires training and physical restraint of the animal. In addition, some degree of warming of the animal is usually used to ensure that the tail blood flow is sufficient for a measurement to be made. Even when minimal external warming is used, the combination of restraint and warming may lead to significant increases in core body temperature (Buñag, 1984). Since both restraint and warming constitute stresses that may affect blood pressure, the values of blood pressure obtained with the tail-cuff technique may reflect not only the animals' general blood pressure level, but also the reactivity of blood pressure to the stress of the procedure.

Direct methods refer to techniques by which arterial blood pressure is measured directly with the aid of a sensor device implanted invasively within the arterial system. The most widely used sensor device in animal studies has been the saline-filled catheter, whose distal end is connected to a calibrated pressure transducer (Van Vliet et al., 2000; Braga et al., 2007). The disadvantages to the fluid-filled catheter method requires rodents to be tethered and handled, catheter patency limitations prevent long-term measurements (i.e., for no longer than one week) and the mobility of the animal is considerably restricted. In addition, there is a potential for infection, potential for loss of catheter patency (e.g., clotting), leading to a degradation or loss of the blood pressure signal, and a limited dynamic response, which makes detection of the true systolic and diastolic pressures challenging in small animals with high heart rates.

The recent development of miniature, implantable radiotelemetric devices offers the possibility of long-term, hands-off blood pressure measurement in untethered rodents living in their home cages (Mills et al., 2000). Implantable telemetry devices suitable for use in small laboratory animals provide several advantages over other methods of blood pressure measurement. These advantages include the ability to obtain blood pressure recordings in conscious, unstressed, freely moving animals, the ability to obtain continuous recordings (24 h/day), the ability to obtain high-fidelity recordings, due to a frequency response that exceeds that of traditional saline-filled catheter systems, and the long-term patency of the catheter, which may be used for many weeks or months without loss of the signal or fidelity of the recordings. Therefore, telemetry has become the “gold standard” for measuring blood pressure in laboratory animals (Kurtz et al., 2005). Figure 1 illustrates a blood pressure tracing acquired using telemetry in a rat.

Original blood pressure tracings from a rat 21 days following implantation of a telemetric device showed in different time scales (0.5, 2 and 30 s).

One important aspect that may limit the use of telemetry is cost. For many investigators with limited funding, the cost of purchasing telemetry equipment and that of the necessary periodic factory refurbishment of telemeters may be prohibitive. Companies are working on developing more cost-effect devices, but they still have a long way to go. However, for chronic experiments, telemetry may be cost-effective when compared to other methods.

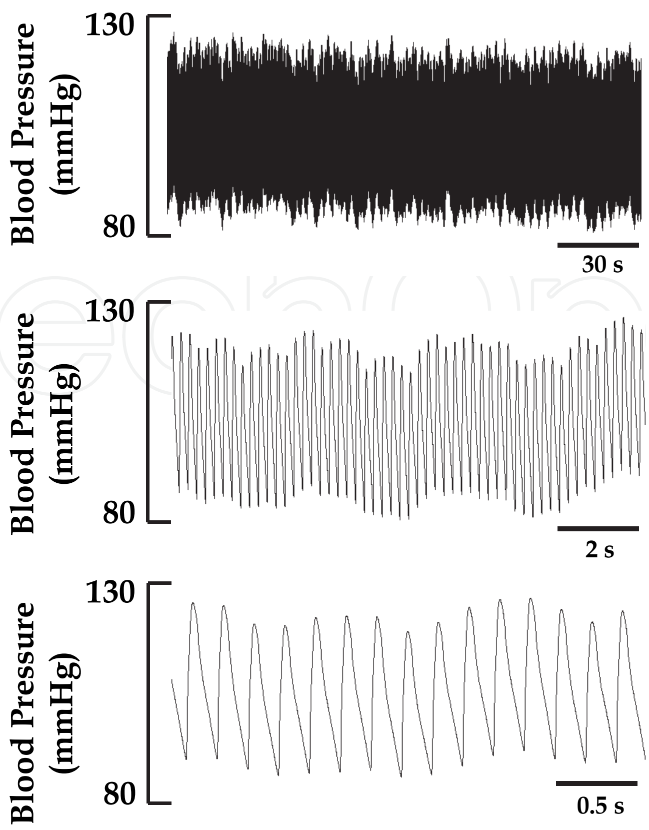

Fig. 1. The feasibility of telemetry for accurate blood pressure measurement.

Relative to a chronic catheter, tether, and swivel system in laboratory animals, the telemetry system requires little day-to-day maintenance, however, and may, therefore, be less labor-intensive and lead to savings in this regard. On the other hand, the cost of factory refurbishment of telemeters depends very much on the pattern of use of the telemetry devices and may represent high costs to researchers. The average nominal battery life of telemeters is 6-8 months depending on the model. However, battery life can be extended by turning off the telemeter when not in use by the use of a magnetic switch, allowing the battery life to be distributed over a longer period of time. More importantly, with care, the telemeter can be explanted, cleaned, recalibrated, resterilized, and reimplanted a number of times without factory refurbishment, thereby maximizing the use of the device and minimizing the cost incurred per animal. The extent to which the telemeters can be reused before refurbishment will depend on the nature and length of the experimental protocol, as well as the care used in implanting and explanting the device. Thus, telemeters can be particularly cost effective when used for multiple short-term implants in rats, with refurbishment costs dropping below US$20 per implantation (Van Vliet et al., 2000).

2.1 Application of telemetry for studying hypertension

The advent of commercially available wireless telemetric technology for blood pressure measurements in laboratory animals has been a significant advancement in hypertension research. The technique has been widely validated and is now available for use in virtually all laboratory animals from mice to monkeys. Of note, its greatest use thus far has been in the rat, the species that has most frequently been used in cardiovascular research.

Telemetric devices have the advantage of allowing for chronic, direct and accurate measurements of blood pressure without the need for restraint. Because of their unlimited capacity for continuous data acquisition over months, telemetry systems also provide the ability to measure blood pressure 24 hours per day, 7 days per week. As a result, continuous direct measurements of blood pressure using telemetry permit diurnal variations in blood pressure to be quantified.

In mammals, the circadian rhythms of behaviour, physiology and metabolism are generated by an internal biological clock mainly located in the suprachiasmatic nucleus of the anterior hypothalamus (Meijer & Rietveld, 1989). The endogenous timekeeping function of the suprachiasmatic nucleus is complemented by its role in the entrainment of circadian rhythms to environmental stimuli. Among the numerous environmental factors acting as synchronizers for the entrainment of endogenous circadian rhythms, the daily light/dark cycle appears to be the most potent factor (Morin, 1994). The information about light/dark cycle is transmitted from the retina to the suprachiasmatic nucleus, which drives the daily rhythm in secretion of the pineal hormone, melatonin (Rusak & Bina, 1990; Morin, 1994), and allows organisms to synchronize the circadian rhythms of behaviour and physiology.

Arterial blood pressure and heart rate exhibit circadian rhythms in both animals (Van Den Buuse, 1994) and humans (Mancia et al., 1983). Specifically, blood pressure and heart rate are lower during periods of rest compared to those of activity, which is related to the day/night rhythm (Conway et al., 1984). In addition, it is well known that life-threatening cardiovascular events such as sudden cardiac death, stroke and myocardial infarction most frequently occur in the early morning hours and are related to the seasonal changes (Marler et al., 1989; Chasen & Muller, 1998). Although various mechanisms may be responsible for these disturbances, they all appear to coincide with the period of increase in the 24-h blood pressure rhythm (Muller et al., 1989).

The advent of telemetry has helped to elucidate how the circadian rhythm influences blood pressure and heart rate in laboratory animals. For example, studies by Zang et al. (2000) demonstrated that rats exposed to a reduction in the photoperiod by changing the light/dark ratio from 12/12h to 8/16h presented altered blood pressure and heart rate variations in a 24h-cycle and that the magnitude of the changes depended on the direction of the extension of the dark period. In addition, transgenic rats with a deficit in brain angiotensin presented a poor adaptation to changes in light/dark cycles when compared to rats with an intact brain renin-angiotensin system (Campos et al., 2006). Furthermore, spontaneously hypertensive rats instrumented with telemeters and treated with various beta blockers displayed gender differences in regards to the drugs' effects on daily variations in blood pressure and heart rate (Grundt et al., 2006). Along these lines, studies employing telemetry demonstrated that treatment with angiotensin-(1-7) agonist alters the circadian rhythm and baroreflex control in spontaneously hypertensive rats (Wessel et al., 2007). In addition to the studies performed in rats, telemetry studies have demonstrated that type 2 diabetic mice exhibit hypertension and disrupted blood pressure and heart rate oscillations during the normal circadian rhythm (Su et al., 2008). Figure 2 shows data generated from recording blood pressure using telemetry for one hour during the day and one hour during the night in a group of rats, illustrating the ability to evaluate diurnal and nocturnal variations in blood pressure.

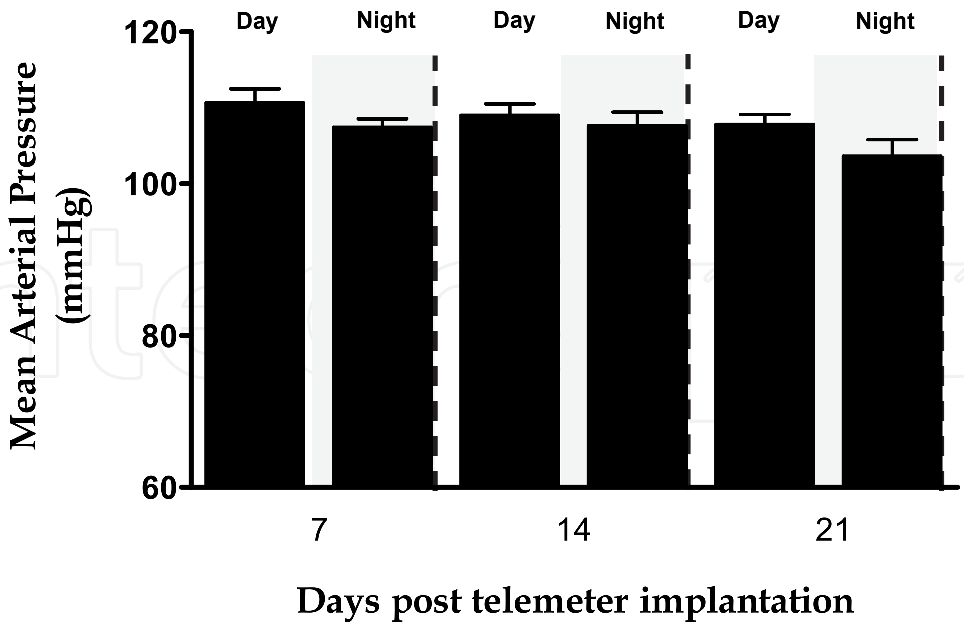

Fig. 2. Effect of the circadian rhythm on blood pressure variations.

Blood pressure values from a group of rats acquired during the day and during the night over 21 days illustrating the application of telemetry for studying diurnal and nocturnal blood pressure variations.

The convenience and reliability of telemetry methodology in cardiovascular research are reflected in the increasing frequency of its utilization by laboratories worldwide. In addition to its application for establishing the extent and duration of the cardiovascular effects of pharmaceutical agents, it has been applied to address unanswered questions in which conventional indirect measurements had yielded inconsistent and often conflicting data. More importantly, it has opened new areas of investigation such as long-term neuro-humoral and cardiovascular regulation of blood pressure and its variability, which were previously beyond the limitations of indirect measurement techniques in rats and mice.

One important application of telemetry is in understanding the pathogenesis of hypertension-associated target organ damage. Although it is generally believed that hypertension contributes to target organ damage, the quantitative relationships have remained controversial since target organ damage is a complex phenomenon thought to be influenced by both blood pressure-dependent and -independent mechanisms. For example, studies performed by Supowit et al. (2005) employing telemetry for studying hypertension-induced end organ damage in hypertensive alpha-calcitonin gene-related peptide knockout mice demonstrated that these transgenic mice presented marked vasculitis in the heart with thickening and inflammation of the vessel walls when compared to hypertensive wild type controls. In addition, transgenic mice presented myocarditis and focal epicarditis with areas of myocardial necrosis. Moreover, the kidneys of these transgenic mice exhibited prominent glomerular changes including congestion of the capillary loops, focal mesangial and crescent proliferation, and focal histocytic infiltration. Finally, urinary microalbumin was significantly higher in the hypertensive alpha-calcitonin gene-related peptide knockout compared to hypertensive wild-types. These findings suggest that deletion of the alpha-calcitonin gene-related peptide gene renders the heart and kidneys more vulnerable to hypertension-induced end organ damage.

Recently, telemetry has been employed for chronic blood pressure measurements up to several months in transgenic, knockout and inbred mouse strains in order to identify the mechanisms underlying different forms of hypertension. Figure 3 shows the development of hypertension in a mouse model of essential hypertension achieved by chronic infusion of angiotensin-II, where blood pressure has been measured daily for 21 days.

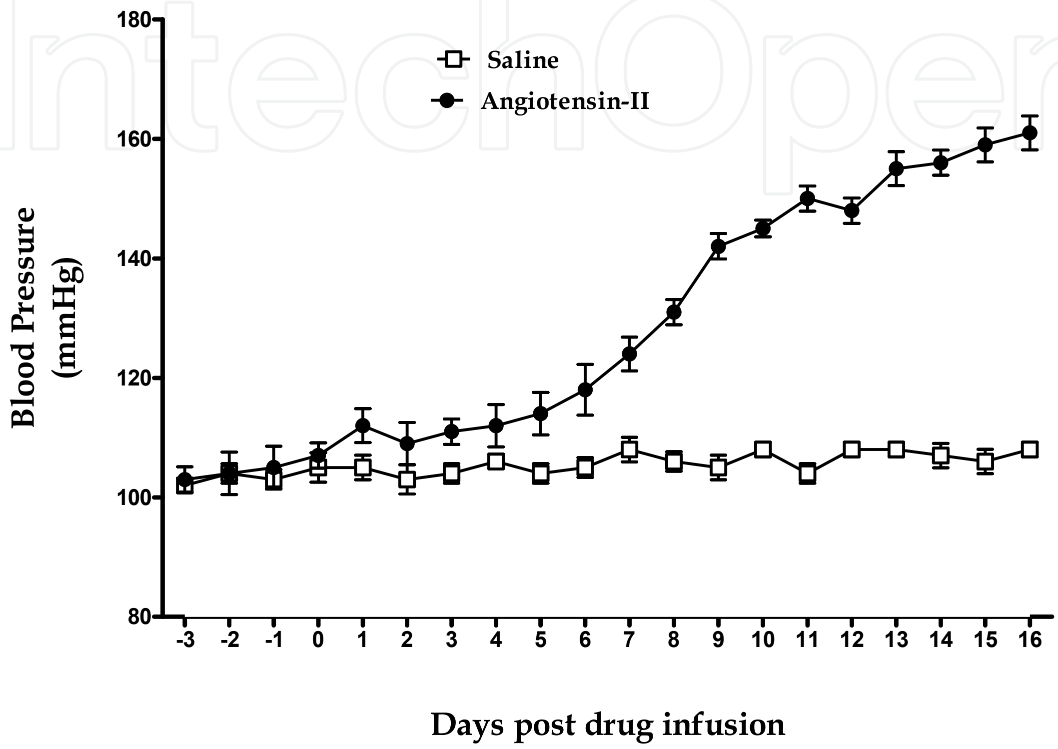

Fig. 3. Use of telemetry in experimental models of hypertension.

Daily blood pressure showing the gradual development of angiotensin-II-dependent hypertension in mice instrumented with telemetric devices and subcutaneously infused with saline or angiotensin-II.

One of the first studies reporting the application of telemetry for studying hypertension in mice was performed by Carlson & Wyss (2000). While developing the technique, the authors demonstrated that although carotid and aortic placements of the telemetry probe provided equally accurate monitoring of arterial pressure and heart rate, the carotid placement yielded a much greater success rate. They also demonstrated that exposure to a high salt diet increased both the amplitude of the arterial pressure rhythm and the average mean arterial pressure, as would be predicted from previous studies in salt-resistant rats. These findings indicated that telemetric recording of long-term arterial pressure and heart rate could be a powerful tool with which to define the mechanisms underlying hypertension in mice. Subsequent studies by Butz & Davisson (2001) further extended the use of telemetry for dissecting the mechanisms underpinning hypertension to pregnant and non-pregnant transgenic and wild type mice. Specifically, they demonstrated the feasibility of continuously monitoring blood pressure before, during and after pregnancy in mice via left carotid artery implantation, which did not interfere with conception, gestation, delivery or postnatal care of pups.

Following these pioneering studies, which set the ground for using telemetry in mice to understand mechanisms underlying hypertension, many other studies combined the advantages of telemetry with the increasing ability to easily and rapidly develop transgenic mouse strains. For example, telemetry has been used to examine hypertension, heart rate variability and baroreflex sensitivity in angiotensin-2-dirupted mice (Gross et al., 2000), hypertension in beta-adducin-deficient mice (Marro et al., 2000),]circadian rhythm effects on blood pressure in eNOS-knockout mice (Van Vliet et al., 2003), menopause-associated hypertension in follitropin receptor knockout mice (Javeshghani et al., 2003), hypertensive response to acute stress in interleukin-6 knockout mice (Lee et al., 2004), hypertension in D4 dopamine receptor-deficient mice (Bek et al., 2006), endothelial dysfunction and elevated blood pressure in MAS gene-deleted mice (Xu et al., 2008), and so on. We recently published an article where we associated virus-mediated gene transfer to the central nervous system, blood pressure recordings using telemetry, and in vivo bioluminescence technology for longitudinal tracking the expression of the redox-regulated activation of activator protein-1 (AP-1), a nuclear transcriptional factor, during the development of renovascular hypertension in mice (Burmeister et al., 2011). Therefore, there are unlimited possibilities for employing different technique combinations associated to telemetry to unravel the mechanisms underlying hypertension.

2.2 Scientific articles Involving telemetry for studying hypertension

The number of articles published using telemetry to study hypertension in mice has steadily increased in the last decade. Figure 4A shows the evolution of the number of articles published in Pubmed (www.pubmed.com) from 2000 to 2010 using the key words “telemetry”, “hypertension” and “mice”. This number is even greater if the key word “hypertension” is changed to “blood pressure” (Figure 4B), and other combinations yield different numbers. Interestingly, this positive trend seems to be reversing with regard to studies using rats, as illustrated in Figures 5A and 5B.

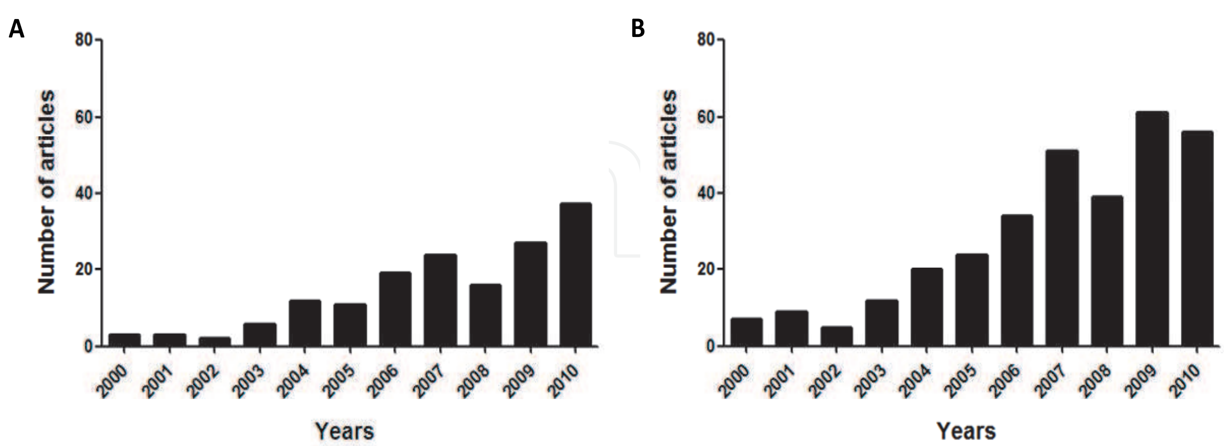

Fig. 4. Publications involving telemetry and mice.
A. Number of articles published in Pubmed from 2000 to 2010 found using the key words “telemetry, hypertension and mice.” B. Number of articles published in Pubmed from 2000 to 2010 searched using the key words “telemetry, blood pressure and mice”.

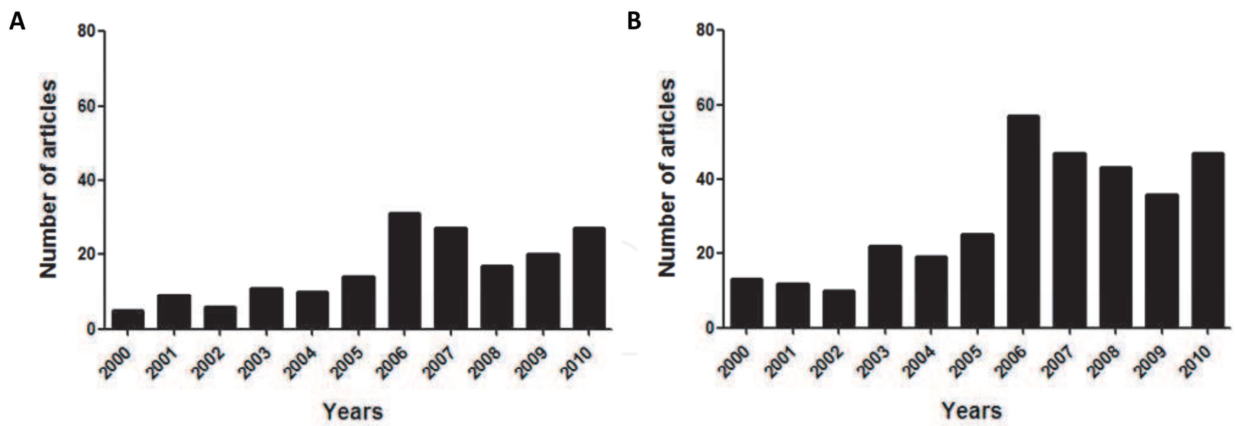

Fig. 5. Publications involving telemetry and rats.
A. Number of articles published in Pubmed from 2000 to 2010 found using the key words "telemetry, hypertension and rat." B. Number of articles published in Pubmed from 2000 to 2010 found using the key words "telemetry, blood pressure and rat."

3. Contribution of telemetry for the animal welfare and refinement

Promoting animal welfare by minimizing pain and distress are important factors to consider in order to acquiring reliable and physiologically accurate results from experimental rodent models of hypertension, as for any other disease models. It is widely recognized that telemetry can reduce stress to animals since it reduces or eliminates the requirement for external instrumentation, restraint or tethering. Telemetry also provides objective biological evidence of animal well-being such as variations in heart rate, blood pressure and body temperature, variations in which may reflect acute or chronic discomfort, stress, distress, pain and fear. In addition, the return of variables such as heart rate to normal circadian rhythms can be used as indicators of physiological recovery and readiness for experimental procedures. When compared to other conventional cardiovascular measurement methods, telemetry offers several advantages including, but not limited to, the 1) elimination of the confounding effects of stress introduced by handling, restraint and anaesthesia; 2) reduction in the number of animals used by 60% to 70%; and (c) unrestricted collection of continuous data for months without the need for any additional manipulation.

The effect of telemetry on an animal's welfare depends on the nature of the technique chosen for implantation and the mass and volume of the device. One of the classic methods described for telemetric device implantation is the abdominal aorta approach, where the blood pressure catheter is inserted into the abdominal aorta, while the body of the transmitter is positioned in the peritoneal cavity (Mills et al., 2000). This method has been refined since it was first proposed. For example, studies performed by Johnston et al. (2007) have assessed the effect of several interventions on postsurgical recovery of food and water intake, core body temperature and locomotor activity. Whereas some of the interventions were associated with increased mortality (such as administration of the postoperative xylazine reversal agent atipamezole), others were either detrimental (such as use of the abdominal lubricant carboxymethylcellulose) or had little or no effect on recovery (such as thermal support).

An alternative approach to the abdominal aorta method places the pressure sensing catheter in the aorta, via the left carotid artery, and the transmitter body subcutaneously on the back at the midscapular region (Carlson & Wyss, 2000) or along the right flank (Butz & Davisson, 2001). Studies from Kaidi et al. (2007) compared the two different techniques in mice. The authors demonstrated that, in left carotid-implanted mice, 80% survived surgery and recovered well. In contrast, only 57% of mice implanted with the abdominal aortic technique survived surgery, and some presented lethal complications. Both techniques had similar recovery times for body weight and food consumption, with a comparable return of normal circadian rhythm by day 6 post-surgery and similar cardiovascular baseline values. Six out of the eight left carotid-implanted mice remained in good health and had good pressure signal for at least 100 days post-surgery, while most of the abdominal aortic-implanted mice had lost the pressure signal within 14–49 days post-surgery. The authors concluded that left carotid artery implantation in mice is superior to the abdominal aorta technique and is more appropriate for long-term telemetry studies, especially in smaller animals. In agreement with this, Butz & Davisson (2001) suggested the use of the left carotid artery implantation approach for studies involving pregnant mice.

In addition to the surgical technique employed for implanting the device, the mass of the implanted device is equally important. Adding additional mass to an animal's body can have significant physiologic effects and can cause distress and discomfort, particularly in small species such as rodents. For instance, increasing the mass in abdominal viscera can compromise diaphragmatic movement and alter breathing pattern. In the short term, changes in body mass and behavior after implantation surgery in mice indicate that their well-being is impaired during the first days after surgery. An animal may require 5 to 7 days to regain its normal circadian rhythm (Butz & Davisson, 2001). Restoration of well-being follows the same time course in rats implanted with transmitters. Therefore, telemetric devices should be as lightweight as possible, although it may be difficult to establish general principles on the appropriate device size and mass.

Considering that the size and shape of the device must avoid or minimize any compromise of normal physiologic function or welfare of the animal, the use of telemetric devices designed for mice in rats affords some remarkable advantages as described by Braga & Prabhakar (2009). For example, implantation of the smaller telemeter is easier because the diameter of the catheter tip is smaller than that for the device designed for rats, thus, facilitating insertion into the abdominal aorta. Another important advantage is the size of the animal that can be implanted: the mouse telemeter can be implanted in animals as small as 17 g, whereas the rat telemeter is only appropriate for animals weighing at least 175 g. Therefore, the approach proposed by Braga & Prabhakar (2009) would be useful for blood pressure studies in neonates and young rats. In addition, the mouse device occupies much less space in the abdominal cavity, as shown in Figure 6, allowing for better accommodation of the internal organs around the transmitter. This feature would be particularly relevant for researchers investigating cardiovascular physiology and physiopathology during pregnancy (such as pre-eclampsia). As important disadvantages to consider, the transmitters designed for mice are more expensive and have a considerably shorter battery life than do the rat transmitters. The costs for a long-term experiment might be increased by 70% to 100% when using the mice transmitter. The main points that must be taken into account for designing such studies are the battery life of the mice transmitter, which is about 6 wk of continuous recording (compared to 17 wk for the rat transmitter), and the costs for refurbishing the transmitter (that is, replacing catheters and recharging batteries) are considerably higher.

These advantages and disadvantages should be taken into consideration when designing chronic experiments using different transmitter types.
It is important to highlight that telemetry improves data quality and quantity, which can lead to a reduction in the number of animals required for each study. In toxicology and pharmacology, telemetry may also be able to identify dose-limiting effects of a compound evidenced by subtle changes in blood pressure or heart rate so that higher dosing studies are not required. However, reducing animal numbers can also increase animal suffering, and it is important to be aware of this and make sure that it does not happen. For example, as implant miniaturization has progressed, sensor functionality has increased such that individual devices may increase in size because more parameters are being measured. Larger batteries may be required, which also makes devices more bulky. These devices will be heavier and require more invasive surgery to implant them. Therefore, it is imperative to ensure that animal numbers have been reduced as far as possible by taking the better quality and quantity of data obtained using telemetry into account when designing experiments. It also important to recognize that there can be a 'trade off' between reduction and refinement, e.g. where fewer animals are used but devices are more bulky or complex. Finally, the impact on each animal should be considered, and reducing numbers at the expense of individual suffering avoided.

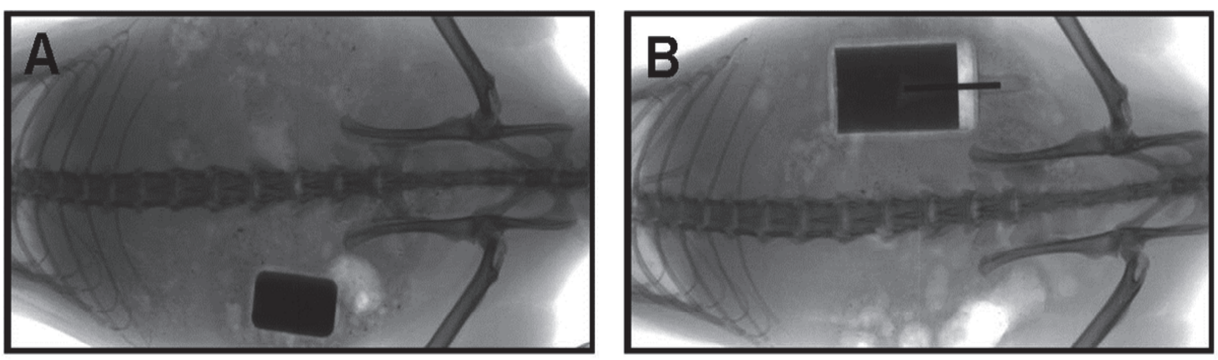

Fig. 6. Refinement of the surgical approach and size of the implanted device.

Radiographic pictures acquired from two different rats implanted with either the mouse (A) or the rat telemetric device (B). Pictures are from first author's personal collection.
New developments in telemetry research can lead to refinements in procedures and/or reductions in animal numbers so it is essential to ensure that progress is monitored and techniques and equipment are updated whenever possible. Some ways to keep updated are using the World Wide Web and attending telemetry user group meetings. It is, however, important to use information from the web or user groups very critically, as it may not be properly refereed or refereed at all. Uncritical use could lead to welfare problems or undermine scientific validity. Further information on refinement husbandry and telemetry procedures for measuring blood pressure in laboratory animals have been described in details by Morton et al. (2003) and Hawkins et al. (2004).

4. Conclusion

Here we have reviewed how advancements in telemetric monitoring of blood pressure and heart rate have led to several major discoveries in the field of cardiovascular research, primarily hypertension and associated pathologies. The benefits of telemetry as a reliable method for measuring in vivo blood pressure in small laboratory animals are further heightened by the advantages that the technique provides regarding cost effectiveness and animal welfare. Until recently, the most commonly used techniques for monitoring blood pressure in conscious rats and mice were a tail cuff device or an exteriorized catheter connected to a pressure transducer. There are, however, considerable drawbacks associated with each of these methods that make them undesirable as accurate means of obtaining blood pressure measurements. Namely, the accuracy of blood pressure measurements using tail cuff are significantly affected by environmental factors as well as by any physiological or pharmacological factor that influences blood flow in the tail, nor does the method allow for continuous blood pressure recordings. Although exteriorized catheters do allow for blood pressure to be measured continuously, decreasing catheter patency is a problem that usually limits the duration of reliable recordings.

Physiologic data collection using telemetry has many advantages over older methods such as restraints, cuffs, tethers, etc. Data are free from physiological and psychological stress- and anaesthesia-induced artefact. Furthermore, telemetry is more cost-effective and less labor-intensive when compared to tail cuff and exteriorized catheters, and there is an increased chance of capturing occasional and transient events over a long period. There is also a reduction in the number of animals required due to more and better quality data. As a result, the technique has proven to be an extremely valuable tool for researchers, especially those in the fields of cardiovascular physiology and pharmacology, where the use of telemetry for measuring blood pressure, cardiac activity, heart rate, body temperature and locomotor activity in rodents has been sufficiently validated.

Continually evolving refinements in telemetry methodology will undoubtedly aid researchers in acquiring high quality, physiologically relevant data and contribute to groundbreaking discoveries that may, ultimately, lead to therapeutics.

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6. References

Bek, M.J., Wang, X., Asico, L.D., Jones, J.E., Zheng, S., Li, X., Eisner, G.M., Grandy, D.K., Carey, R.M., Soares-da-Silva, P. & Jose, P.A. (2006). Angiotensin-II type 1 receptor-mediated hypertension in D4 dopamine receptor-deficient mice. *Hypertension*, Vol. 47, No. 2, pp. 288-95, ISSN 0194-911X.

Braga, V.A., Soriano, R.N., Braccialli, A.L., de Paula, P.M., Bonagamba, L.G., Paton, J.F. & Machado, B.H. (2007). Involvement of L-glutamate and ATP in the neurotransmission of the sympathoexcitatory component of the chemoreflex in the commissural nucleus tractus solitarii of awake rats and in the working heart-brainstem preparation. *The Journal of Physiology*, Vol. 581, No. 3, pp. 1129-45, ISSN 0022-3751.

Braga, V.A. & Prabhakar, N.R. (2009). Refinement of telemetry for measuring blood pressure in conscious rats. *Journal of the American Association for Laboratory Animal Science*, Vol. 48, No. 3, pp. 268-71, ISSN 1060-0558.

Burmeister, M.A., Young, C.N., Braga, V.A., Butler, S.D., Sharma, R.V. & Davisson, R.L. (2011). In vivo bioluminescence imaging reveals redox-regulated activator protein-1 activation in paraventricular nucleus of mice with renovascular hypertension. *Hypertension*, Vol. 57, No. 2, pp. 289-97, ISSN 0194-911X.

Buñag, R.D. (1984). Measurement of blood pressure in rats. In: W. de Jong (Ed.), Handbook of Hypertension, Volume 4: Experimental and genetic models of hypertension (pp. 1–12). Elsevier, New York, ISBN 0444897151.

Butz, G.M. & Davisson, R.L. (2001). Long-term telemetric measurement of cardiovascular parameters in awake mice: a physiological genomics tool. *Physiological Genomics*, Vol. 5, No. 2, pp. 89-97, ISSN 1094-8341.

Campos, L.A., Plehm, R., Cipolla-Neto, J., Bader, M. & Baltatu, O.C. (2006). Altered circadian rhythm reentrainment to light phase shifts in rats with low levels of brain angiotensinogen. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, Vol. 290, No. 4, pp. R1122-7, ISSN 0363-6119.

Carlson, S.H. & Wyss, J.M. (2000). Long-term telemetric recording of arterial pressure and heart rate in mice fed basal and high NaCl diets. *Hypertension*, Vol. 35, No. 2, pp. E1-5, ISSN 0194-911X.

Chasen, C. & Muller, J.E. (1998). Cardiovascular triggers and morning events. *Blood Pressure Monitoring*, Vol. 3, No. 1, pp 35–42, ISSN 1359-5237.

Conway, J., Boon, N., Davies, C., Jones, J.V. & Sleight, P. (1984). Neural and humoral mechanisms involved in blood pressure variability. *Journal of Hypertension*, Vol. 2, No. 1, pp. 203–208, ISSN 0263-6352.

Gauvin, D.V., Tilley, L.P., Smith, F.W. Jr. & Baird, T.J. (2006). Electrocardiogram, hemodynamics, and core body temperatures of the normal freely moving laboratory beagle dog by remote radiotelemetry. *Journal of Pharmacological and Toxicological Methods*, Vol. 53, No. 2, pp. 128-39, ISSN 1056-8719.

Greene, A.N., Clapp, S.L. & Alper, R.H. (2008). Timecourse of recovery after surgical intraperitoneal implantation of radiotelemetry transmitters in rats. *Journal of Pharmacological and Toxicological Methods*, Vol. 56, No. 2, pp. 218-22, ISSN 1056-8719.

Gross, V., Milia, A.F., Plehm, R., Inagami, T. & Luft, F.C. (2000). Long-term blood pressure telemetry in AT2 receptor-disrupted mice. *Journal of Hypertension*, Vol. 18, No. 7, pp. 955-61, ISSN 0263-6352.

Grundt, C., Meier, K. & Lemmer, B. (2006). Gender dependency of circadian blood pressure and heart rate profiles in spontaneously hypertensive rats: effects of beta-blockers. *Chronobiology International*, Vol. 23, No. 4, pp. 813-29, ISSN 0742-0528.

Hawkins, P., Morton, D.B., Bevan, R., Heath, K., Kirkwood, J., Pearce, P., Scott, L., Whelan, G., Webb, A. & Joint Working Group on Refinement. (2004). Husbandry refinements for rats, mice, dogs and non-human primates used in telemetry procedures. Seventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement, Part B. *Laboratory Animals*, Vol. 38, No. 1, pp. 1-10, ISSN 0023-6772.

Hess, P., Rey, M., Wanner, D., Steiner, B. & Clozel, M. (2007) Measurements of blood pressure and electrocardiogram in conscious freely moving guineapigs: a model for screening QT interval prolongation effects. *Laboratory Animals*, Vol. 41, No. 4, pp. 470-80, ISSN 0023-6772.

Hoffmann, D.S., Weydert, C.J., Lazartigues, E., Kutschke, W.J., Kienzle, M.F., Leach, J.E., Sharma, J.A., Sharma, R.V. & Davisson, R.L. (2008). Chronic tempol prevents hypertension, proteinuria, and poor feto-placental outcomes in BPH/5 mouse model of preeclampsia. *Hypertension*, Vol. 51, No. 4, pp. 1058-65, ISSN 0194-911X.

Javeshghani, D., Touyz, R.M., Sairam, M.R., Virdis, A., Neves, M.F. & Schiffrin, E.L. (2003). Attenuated responses to angiotensin II in follitropin receptor knockout mice, a model of menopause-associated hypertension. *Hypertension*, Vol. 42, No. 4, pp. 761-7, ISSN 0194-911X.

Johnston, N.A., Bosgraaf, C., Cox, L., Reichensperger, J., Verhulst, S., Patten, C. Jr & Toth, L.A. (2007). Strategies for refinement of abdominal device implantation in mice: strain, carboxymethylcellulose, thermal support, and atipamezole. *Journal of the American Association for Laboratory Animal Science*, Vol. 46, No. 2, pp. 46-53, ISSN 1060-0558.

Kaïdi, S., Brutel, F., Van Deun, F., Kramer, K., Remie, R., Dewé, W., Remusat, P., Delaunoism A. & Depelchin, O. (2007). Comparison of two methods (left carotid artery and abdominal aorta) for surgical implantation of radiotelemetry devices in CD-1 mice. *Laboratory Animals*, Vol. 41, No. 3, pp. 388-402, ISSN 0023-6772.

Kim, H.S., Krege, J.H., Kluckman, K.D., Hagaman, J.R., Hodgin, J.B., Best, C.F., Jennette, J.C., Coffman, T.M., Maeda, N. & Smithies, O. (1995). Genetic control of blood pressure and the angiotensinogen locus. *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 92, No. 1, pp. 2735–2739, ISSN 0027-8424.

Kramer, K., Kinter, L., Brockway, B.P., Voss, H.P., Remie, R. & Van Zutphen, B.L. (2001). The use of radiotelemetry in small laboratory animals: recent advances. *Contemporary Topics in Laboratory Animal Science*, Vol. 40, No. 1, pp. 8-16, ISSN 1060-0558.

Kramer, K. & Kinter, L.B. (2003). Evaluation and applications of radiotelemetry in small laboratory animals. *Physiological Genomics*, Vol. 13, No. 3, pp. 197-205, ISSN 1094-8341.

Kurtz, T.W., Griffin, K.A., Bidani, A.K., Davisson, R.L., Hall, J.E. AHA Council on High Blood Pressure Research, Professional, & Public Education Subcommittee. (2005). Recommendations for blood pressure measurement in animals: summary of an AHA scientific statement from the Council on High Blood Pressure Research, Professional, and Public Education Subcommittee. *Arteriosclerosis, Thrombosis, and Vascular Biology*, Vol. 25, No. 1, pp. 478–479, ISSN 1079-5642.

Lee, D.L., Leite, R., Fleming, C., Pollock, J.S., Webb, R.C. & Brands, M.W. (2004). Hypertensive response to acute stress is attenuated in interleukin-6 knockout mice. *Hypertension*, Vol. 44, No. 3, pp. 259-63, ISSN 0194-911X.

Mancia, G., Ferrari, A., Gregorini, L., Parati, G., Pomidossi, G., Bertinieri, G., Grassi, G., Di Rienzo, M., Pedotti, A. & Zanchetti, A. (1983). Blood pressure and heart rate variabilities in normotensive and hypertensive human beings. *Circulation Research*, Vol 53, No. 1, pp 96–104, ISSN 0009-7330.

Marler, J.R., Price, T.R. & Clark, G.L. (1989). Morning increases in onset of ischemic stroke. *Stroke*, Vol. 20, No. 1, pp. 473–476Meijer, J.H. & Rietveld, W.J. (1989). Neurophysiology of the suprachiasmatic circadian pacemaker in rodents. *Physiological Reviews*, Vol. 69, No. 1, pp. 671–707, ISSN 0031-9333.

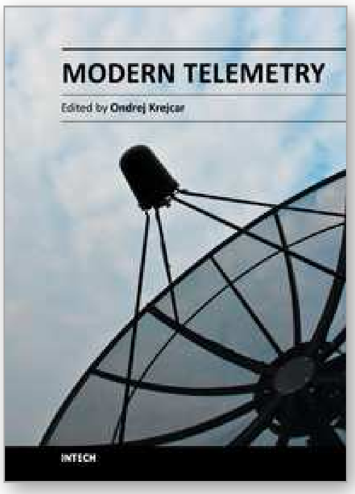
Marro, M.L., Scremin, O.U., Jordan, M.C., Huynh, L., Porro, F., Roos, K.P., Gajovic, S., Baralle, F.E. & Muro, A.F. (2000). Hypertension in beta-adducin-deficient mice. *Hypertension*, Vol. 36, No. 3, pp. 449-53, ISSN 0194-911X.

Meijer, J.H. & Rietveld, W.J. (1989). Neurophysiology of the suprachiasmatic circadian pacemaker in rodents. *Physiologival Reviews*, Vol. 69, No. 3, pp. 671-707, ISSN 0031-9333.

Mills, P.A., Huetteman, D.A., Brockway, B.P., Zwiers, L.M., Gelsema, A.J.M., Schwartz, R.S. & Kramer, K. (2000). A new method for measurement of blood pressure, heart rate, and activity in the mouse by radiotelemetry. *Journal of Applied Physiology*, Vol. 88, No. 1, pp. 1537–1544, ISSN 8750-7587.

Moons, C.P., Hermans, K., Remie, R., Duchateau, L. & Odberg, F.O. (2007). Intraperitoneal versus subcutaneous telemetry devices in young Mongolian gerbils (Meriones unguiculatus). *Laboratory Animals*, Vol. 41, No. 2, pp. 262-9, ISSN 0023-6772.

Morin, L.P. (1994). The circadian visual system. *Brain Research*, Vol. 67, No. 1, pp. 102–127, ISSN 0006-8993.
Morton, D.B., Hawkins, P., Bevan, R., Heath, K., Kirkwood, J., Pearce, P., Scott, L., Whelan, G., Webb, A., British Veterinary Association Animal Welfare Foundation, Fund for Replacement of Animals in Medical Experiments, Royal Society for the Prevention of Cruelty to Animals & Universities Federation for Animal Welfare. (2003). Refinements in telemetry procedures. Seventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement, Part A. *Laboratory Animals*, Vol. 37, No. 4, pp. 261-99, ISSN 0023-6772.
Muller, J.E., Tofler, G.H. & Stone, P.H. (1989). Circadian variation and triggers of onset of acute cardiovascular disease. *Circulation*, Vol. 79, No. 1, pp. 733–743, ISSN 0009-7322.
Rusak, B. & Bina, K.G. (1990). Neurotransmitters in the mammalian circadian system. *Annual Review of Neuroscience*, Vol. 13, No. 1, pp. 387–401, ISSN 0147-006X.
Shaw, M.B., Herndon, C.D., Cain, M.P., Rink, R.C. & Kaefer, M. (2007). A porcine model of bladder outlet obstruction incorporating radio-telemetered cystometry. *British Journal of Urology International*, Vol. 100, No. 1, pp. 170-4, ISSN 2042-2997.
Su, W., Guo, Z., Randall, D.C., Cassis, L., Brown, D.R., Gong, M.C. (2008). Hypertension and disrupted blood pressure circadian rhythm in type 2 diabetic db/db mice. *American Journal of Physiology - Heart and Circulatory Physiology*, Vol. 295, No.4, pp. H1634-41, ISSN 0363-6135.
Supowit, S.C., Rao, A., Bowers, M.C., Zhao, H., Fink, G., Steficek, B., Patel, P., Katki, K.A. & Dipette, D.J. (2005). Calcitonin gene-related peptide protects against hypertension-induced heart and kidney damage. *Hypertension*, Vol. 45, No. 1, pp. 109-1, ISSN 0194-911X.
Van den Buuse, M. (1994). Circadian rhythms of blood pressure, heart rate, and locomotor activity in spontaneously hypertensive rats as measured with radio-telemetry. *Physiology & Behavior*, Vol. 55, No. 1, pp. 783–787, ISSN 0031-9384.
Van Vliet, B.N., Chafe, L.L., Antic, V., Schnyder-Candrian, S. & Montani, J.P. (2000). Direct and indirect methods used to study arterial blood pressure. *Journal of Pharmacological and Toxicological Methods*, Vol. 44, No. 2, pp. 361-73, ISSN 1056-8719.
Van Vliet, B.N., Chafe, L.L. & Montani, J.P. (2003). Characteristics of 24 h telemetered blood pressure in eNOS-knockout and C57Bl/6J control mice. *The Journal of Physiology*, Vol. 549, No. 1, pp 313-25, ISSN 0022-3751.
Wessel, N., Malberg, H., Heringer-Walther, S., Schultheiss, H.P. & Walther, T.J. (2007). The angiotensin-(1-7) receptor agonist AVE0991 dominates the circadian rhythm and baroreflex in spontaneously hypertensive rats. *Journal of Cardiovascular Pharmacology*, Vol. 49, No. 2, pp 67-73, ISSN 0160-2446.
Xu, P., Costa-Goncalves, A.C., Todiras, M., Rabelo, L.A., Sampaio, W.O., Moura, M.M., Santos, S.S., Luft, F.C., Bader, M., Gross, V., Alenina, N. & Santos, R.A. (2008). Endothelial dysfunction and elevated blood pressure in MAS gene-deleted mice. *Hypertension*, Vol. 51, No. 2, pp. 574-80, ISSN 0194-911X.
Zhang, B.L., Zannou, E. & Sannajust, F. (2000). Effects of photoperiod reduction on rat circadian rhythms of BP, heart rate, and locomotor activity. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, Vol. 279, No. 1, pp. R169-78, ISSN 0363-6119.
Zimmerman, M.C., Lazartigues, E., Sharma, R.V. & Davisson, R.L. (2004). Hypertension caused by angiotensin II infusion involves increased superoxide production in the central nervous system. *Circulation Research*, Vol. 95, No. 2, pp. 210-6, ISSN 0009-7330.



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Telemetry is based on knowledge of various disciplines like Electronics, Measurement, Control and Communication along with their combination. This fact leads to a need of studying and understanding of these principles before the usage of Telemetry on selected problem solving. Spending time is however many times returned in form of obtained data or knowledge which telemetry system can provide. Usage of telemetry can be found in many areas from military through biomedical to real medical applications. Modern way to create a wireless sensors remotely connected to central system with artificial intelligence provide many new, sometimes unusual ways to get a knowledge about remote objects behaviour. This book is intended to present some new up to date accesses to telemetry problems solving by use of new sensors conceptions, new wireless transfer or communication techniques, data collection or processing techniques as well as several real use case scenarios describing model examples. Most of book chapters deals with many real cases of telemetry issues which can be used as a cookbooks for your own telemetry related problems.