Journal of Paediatric Laboratory Medicine

Dissanayake and Phang, J Paediatr Lab Med 2016, 1:e101

Editorial OMICS International

Autonomic Dysfunction: A potential Mechanism in Programmed Hypertension

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Received date: Nov 11, 2016; **Accepted date**: Nov 12, 2016; **Published date**: Nov 16, 2016

Editorial

Hypertension, a disease of deregulation of blood pressure control, is a major risk factor for cardiovascular and cerebrovascular diseases [1] and is reported to affect approximately 40% of people [2]. In addition to the high prevalence and predicted increases incidence of hypertension, successful treatment remains poor and it has been argued that this is partly due to the poor understanding of causative mechanisms. The autonomic nervous system is central to the control of blood pressure and a neurogenic component of hypertension is becoming increasingly realised as several lines of evidence in humans and animal models show convincingly that abnormalities in autonomic control of blood pressure plays a major role in the etiology of disease and cardiovascular mortality. The mammalian nervous system begins its development during fetal life and continues after birth. Therefore, it is thought that both intrauterine and postnatal insults may sensitise and alter the development of different components of the nervous system.

There is a robust body of evidence indicating that a number of different nutritional manipulations or other adverse variations in the prenatal environment program hypertension; this has been shown convincingly in a number of animal models [3]. Whilst the resultant pathophysiology underlying programmed hypertension is uncertain and may be varied, there is evidence for autonomic dysfunction as a possible causative pathophysiological mechanism underlying the development of fetal programming of hypertension.

To date there has been limited interest in autonomic dysfunction as a potential mechanism in programmed hypertension which may be due to historical reasons as well as technical limitations associated with autonomic measurements.

Historically, the kidney was considered the sole contributor of long term blood pressure control, this theory stems from the teachings of the highly influential Guyton model of blood pressure control. Therefore, many of the work investigating programmed hypertension explored kidney dysfunction as a plausible mechanism in determining the etiology of programmed hypertension. Studies investigating the kidney have indeed shown windows of susceptibility to blood pressure programming that appear to occur during the early stages of kidney development, showing a reduction in glomeruli and nephron number [4-6]. However, there is conflicting evidence as studies show hypertension in the absence of reduced nephron number [7] and reduced nephron number with no apparent hypertension [8]. Although it is physiologically plausible that abnormalities in the kidney may be of importance to the etiology of programmed hypertension, the data indicate that while nephron deficit may play a permissive role, it is not the primary cause of programmed hypertension.

Over the last decade technological advancement have greatly improved our ability to accurately quantify or measure autonomic function. Earlier studies investigating blood pressure of programmed rats used more invasive techniques, such as tail cuff plethysmography. It has been postulated that these types of invasive techniques may be inducing a stress response and therefore the observed increased blood pressures may not be reflective of resting hypertension but that of an exaggerated stress response. Animal models have been used extensively to investigate programmed hypertension using a variety of maternal manipulations [3] however only a few have investigated autonomic dysfunction as a potential mechanism. A study by Samuelsson and colleagues [9] showed hypertension and increased sympathetic activity in rat offspring from mothers fed an obesogenic diet during pregnancy. In addition, hypertension and changes to sympathetic activity was established in the juvenile rate indicating that hypertension and changes in autonomic activity arise as a direct consequence of in utero exposure to a maternal obesogenic diet. Similarly, a study investigating a high fat diet in the absence of maternal obesity in rats showed increased sympathetic activity and blood pressure only in response to a stressor [10]. Studies in rabbits also show increased blood pressure and renal sympathetic nerve activity in offspring from mothers that were fed a high fat diet. Furthermore, an exaggerated sympathetic response was seen when these rabbits were exposed to an acute stressor [11].

Non-invasive measures of autonomic function are imperative when translating these effects into human studies. Recent techniques of heart rate variability and blood pressure variability have facilitated the exploration of autonomic dysfunction as a potential mechanism in programmed hypertension. Several studies of growth-restricted children show changes to cardiovascular control, these include altered blood pressure [12], increased pulse rate [13] and change in heart rate fluctuations [14]. Assessment of heart rate variability has shown that infants born small-for-gestational-age (SGA) exhibit increased sympathetic activity at one and three months of age compared to infants born appropriate-for-gestational age [15]. Beyond childhood, in adults born SGA, direct recording of sympathetic nerve traffic using microneurography showed increased sympathetic nerve activity compared to their control counterparts, who did not differ by central adiposity, body mass index or glucose tolerance; therefore metabolic factors did not attribute to the increased sympathetic activity seen in these SGA individuals [16]. Furthermore, a strong association between low birth weight and a shorter pre ejection period, indicative of a stronger sympathetic control of heart rate [17,18] and increased sympathetic activation of the heart has also been reported [17].

In line with these findings, studies have also shown an association between diminished parasympathetic control and increased risk of malignant cardiac arrhythmias and hypertension [19].

Young adults born with extremely low birth weight exhibit a significantly decreased parasympathetic regulatory capacity compared to their control counterparts during their second and third decade of life [19]. Collectively, these studies suggest that increased sympathetic and reduced parasympathetic activity may manifest during early development, and that autonomic dysfunction is a plausible mechanism underlying the increased risk of hypertension in individuals who had intrauterine growth restriction [16,20].

There is increasing evidence for autonomic dysfunction as a potential mechanism in programmed hypertension. However, to explore the exact mechanism by which this occurs requires further experimental investigation incorporating recent techniques in measuring autonomic function.

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