Modelling preeclampsia and its cardiovascular impact

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What happens in the womb during pregnancy can affect the offspring’s short and long-term cardiovascular health. A clear example of this is the impact of preeclampsia (a hypertensive disorder of pregnancy) in the offspring. Preeclampsia is one of the leading causes of maternal and neonatal deaths worldwide, and it is known to increase the likelihood of cardiovascular disease development in the offspring. Moreover, this effect is worsened when preeclampsia takes place on a chronic hypertensive background, known as superimposed preeclampsia. Due to the elevated number of mothers with pre-existing cardiovascular conditions that have increased prevalence of preeclampsia, the burden of this hypertensive disorder is rapidly increasing nowadays, thereby highlighting the need for research in this area.

The association between hypertension during pregnancy and the detrimental cardiovascular impact in the offspring remains to be fully determined, although it is believed that the origin may be impaired placental function. As pregnancy research in humans is extremely challenging due to ethical reasons, the development of an animal model of preeclampsia is critical to understand the deleterious effect that a hypertensive intrauterine environment has on the offspring throughout their lives. The majority of animal models of preeclampsia induce high blood pressure after the placenta has been fully developed. In contrast, our lab has developed an animal model of superimposed preeclampsia that is able to imitate the abnormal development of the placenta that takes place in humans. This model uses pregnant stroke-prone spontaneously hypertensive rats (SHRSP) that are infused with angiotensin II (ANGII) to increase their cardiovascular stress. The dams infused with 700ng/kg/min ANGII at mid-gestation (gestational day 10.5) present higher systolic and diastolic blood pressure, proteinuria and a decreased cardiovascular adaptation to pregnancy compared to control (saline-treated) dams. In addition, placental dysfunction and neonatal growth restriction are observed, similar to the human maternal preeclampsia phenotype.

This model has been instrumental in the investigation of the cardiovascular impact of “preeclampsia-like” conditions on the offspring long-term. This has been carried out by regular measurements of blood pressure and echocardiography in the offspring from weaning up to adulthood. We have shown that ANGII-exposed offspring have increased left ventricular mass early in life which leads to impaired cardiovascular function in their adulthood. In-utero exposure to ANGII causes fractional shortening reduction and increased ratio of early (E) to late (A) ventricular filling velocities (E/A ratio) between weeks 9 to 17 weeks of age compared to controls, which are markers of both systolic and diastolic dysfunction. These results extend our understanding of cardiovascular development and allow an exploration of potential links between preeclampsia and the detrimental programming of the offspring. This animal model has shown that an unfavourable in-utero environment can shape the cardiovascular health of the offspring later in life and has highlighted the importance for monitoring babies, children and adults after pregnancies complicated by preeclampsia. The causes of this cardiovascular effect are yet to be elucidated; however, this model opens the door to a plethora of information that could not only improve neonatal outcomes but also future health for both mother and offspring.

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Competing interests

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